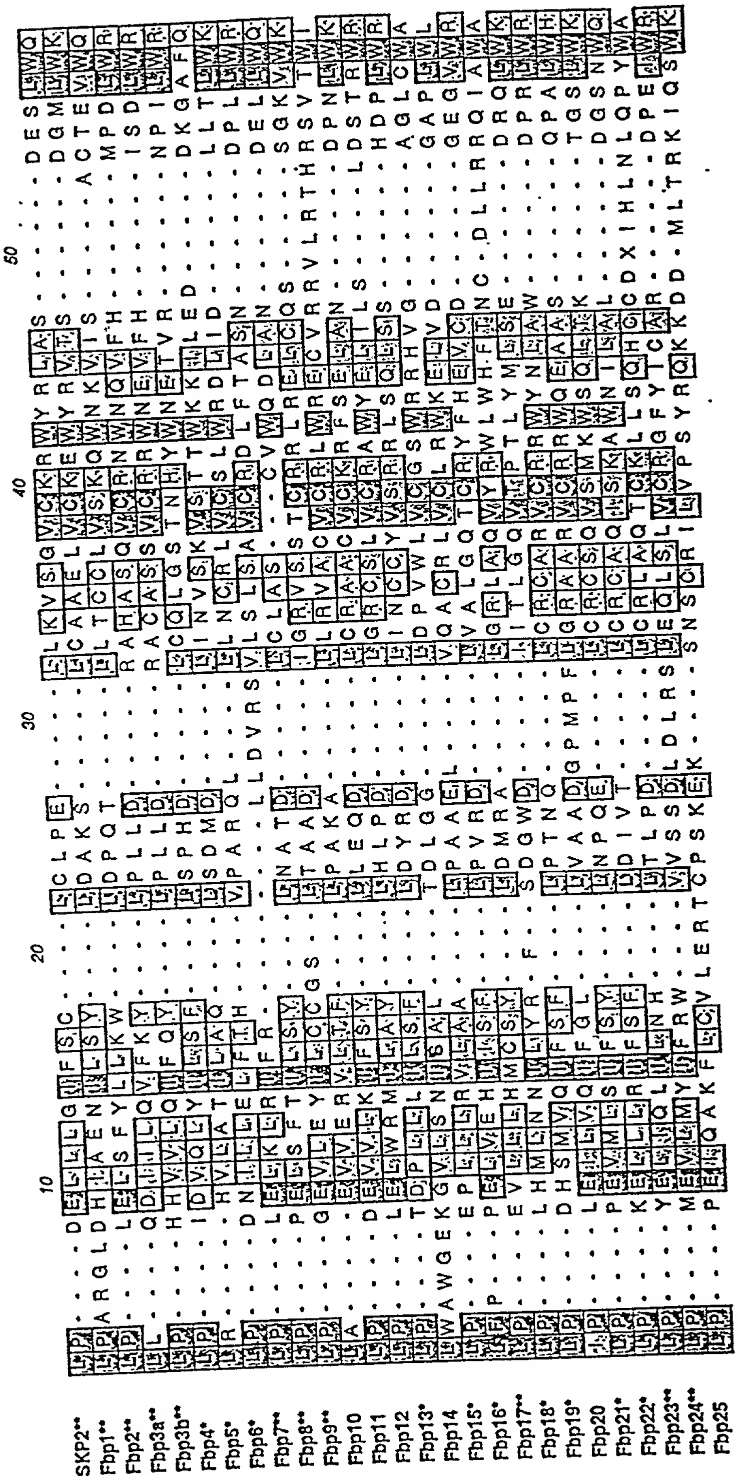
10
20
30
40
50
SKP2**
Fbp1**
Fbp2**
Fbp3a**
Fbp3b**
Fbp4*
Fbp5*
Fbp6*
Fbp7**
Fbp8**
Fbp9**
Fbp10
Fbp11
Fbp12
Fbp13*
Fbp14
Fbp15*
Fbp16*
Fbp17**
Fbp18*
Fbp19*
Fbp20
Fbp21*
Fbp22*
Fbp23**
Fbp24**
Fbp25

FIG. 1

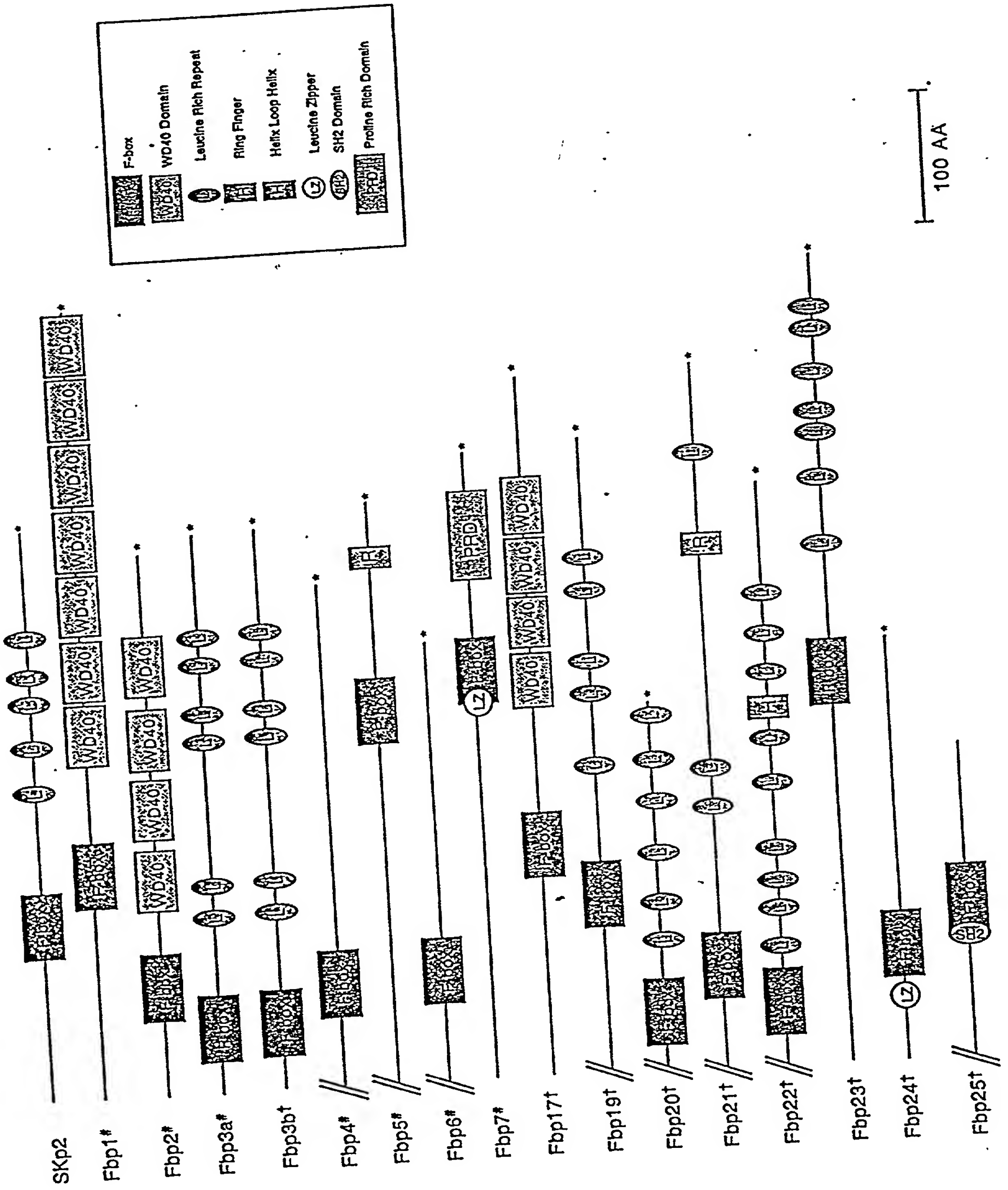
F-box
WD40 Domain
Leucine Rich Repeat
Ring Finger
Helix Loop Helix
Leucine Zipper
SH2 Domain
Proline Rich Domain
100 AA
F-box
WD40
LZ
PRD
SH2
R
H
SKp2
Fbp1#
Fbp2#
Fbp3a#
Fbp3b†
Fbp4#
Fbp5#
Fbp6#
Fbp7#
Fbp17†
Fbp19†
Fbp20†
Fbp21†
Fbp22†
Fbp23†
Fbp24†
Fbp25†

FIG. 2

```
         10        20        30        40        50        60
MDPAEAVLQEKALKFMNSSEREDCNNGEPPRKIIPEKNSLRQTYNSCARLCLNQETVCLA

         70        80        90       100       110       120
STAMKTENCVAKTKLANGTSSMIVPKQRKLSASYEKEKELCVKYFEQWSESDQVEFVEHL

        130       140       150       160       170       180
ISQMCHYQHGHINSYLKPMLQRDFITALPARGLDHIAENILSYLDAKSLCAAELVCKEWY

        190       200       210       220       230       240
RVTSDGMLWKKLIERMVRTDSLWRGLAERRGWGQYLFKNKPPDGNAPPNSFYRALYPKII

        250       260       270       280       290       300
QDIETIESNWRCGRHSLQRIHCRSETSKGVYCLQYDDQKIVSGLRDNTIKIWDKNTLECK

        310       320       330       340       350       360
RILTGHTGSVLCLQYDERVIITGSSDSTVRVWDVNTGEMLNTLIHHCEAVLHLRFNNGMM

        370       380       390       400       410       420
VTCSKDRSIAVWDMASPTDITLRRVLVGHRAAVNVVDFDDKYIVSASGDRTIKVWNTSTC

        430       440       450       460       470       480
EFVRTLNGHKRGIACLQYRDRLVVSGSSDNTIRLWDIECGACLRVLEGHEELVRCIRFDN

        490       500       510       520       530       540
KRIVSGAYDGKIKVWDLVAALDPRAPAGTLCLRTLVEHSGRVFRLQFDEFQIVSSSHDDT

        550       560
ILIWDFLNDPAAQAEPPRSPSRTYTYISR
```

FIG. 3A

```
10 20 30 40 50 60 70 80 90
TGCGTTGGCTGCGGCCTGGCACCAAAGGGGCGGCCCCGGCGGAGAGCGGACCCAGTGGCCTCGGCGATTATGGACCCGGCCGAGGCGGTGCTGC

100 110 120 130 140 150 160 170 180
AAGAGAAGGCACTCAAGTTTATGAATTCCTCAGAGAGAGAAGACTGTAATAATGGCGAACCCCCTAGGAAGATAATACCAGAGAAGAATTCACT

190 200 210 220 230 240 250 260 270 280
TAGACAGACATACAACAGCTGTGCCAGACTCTGCTTAAACCAAGAAACAGTATGTTTAGCAAGCACTGCTATGAAGACTGAGAATTGTGTGGCC

290 300 310 320 330 340 350 360 370
AAAACAAAACTTGCCAATGGCACTTCCAGTATGATTGTGCCCAAGCAACGGAAACTCTCAGCAAGCTATGAAAAGGAAAAGGAACTGTGTGTCA

380 390 400 410 420 430 440 450 460 470
AATACTTTGAGCAGTGGTCAGAGTCAGATCAAGTGGAATTTGTGGAACATCTTATATCCCAAATGTGTCATTACCAACATGGGCACATAAACTC

480 490 500 510 520 530 540 550 560
GTATCTTAAACCTATGTTGCAGAGAGATTTCATAACTGCTCTGCCAGCTCGGGGATTGGATCATATCGCTGAGAACATTCTGTCATACCTGGAT

570 580 590 600 610 620 630 640 650
GCCAAATCACTATGTGCTGCTGAACTTGTGTGCAAGGAATGGTACCGAGTGACCTCTGATGGCATGCTGTGGAAGAAGCTTATCGAGAGAATGG

660 670 680 690 700 710 720 730 740 750
TCAGGACAGATTCTCTGTGGAGAGGCCTGGCAGAACGAAGAGGATGGGGACAGTATTTATTCAAAAACAAACCTCCTGACGGGAATGCTCCTCC

760 770 780 790 800 810 820 830 840
CAACTCTTTTTATAGAGCACTTTATCCTAAAATTATACAAGACATTGAGACAATAGAATCTAATTGGAGATGTGGAAGACATAGTTTACAGAGA

850 860 870 880 890 900 910 920 930 940
ATTCACTGCCGAAGTGAAACAAGCAAAGGAGTTTACTGTTTACAGTATGATGATCAGAAAATAGTAAGCGGCCTTCGAGACAACACAATCAAGA

950 960 970 980 990 1000 1010 1020 1030
TCTGGGATAAAAACACATTGGAATGCAAGCGAATTCTCACAGGCCATACAGGTTCAGTCCTCTGTCTCCAGTATGATGAGAGAGTGATCATAAC

1040 1050 1060 1070 1080 1090 1100 1110 1120
AGGATCATCGGATTCCACGGTCAGAGTGTGGGATGTAAATACAGGTGAAATGCTAAACACGTTGATTCACCATTGTGAAGCAGTTCTGCACTTG

1130 1140 1150 1160 1170 1180 1190 1200 1210 1220
CGTTTCAATAATGGCATGATGGTGACCTGCTCCAAAGATCGTTCCATTGCTGTATGGGATATGGCCTCCCCAACTGACATTACCCTCCGGAGGG

1230 1240 1250 1260 1270 1280 1290 1300 1310
TGCTGGTCGGACACCGAGCTGCTGTCAATGTTGTAGACTTTGATGACAAGTACATTGTTTCTGCATCTGGGGATAGAACTATAAAGGTATGGAA

1320 1330 1340 1350 1360 1370 1380 1390 1400 1410
CACAAGTACTTGTGAATTTGTAAGGACCTTAAATGGACACAAACGAGGCATTGCCTGTTTGCAGTACAGGGACAGGCTGGTAGTGAGTGGCTCA

1420 1430 1440 1450 1460 1470 1480 1490 1500
TCTGACAACACTATCAGATTATGGGACATAGAATGTGGTGCATGTTTACGAGTGTTAGAAGGCCATGAGGAATTGGTGCGTTGTATTCGATTTG

1510 1520 1530 1540 1550 1560 1570 1580 1590
ATAACAAGAGGATAGTCAGTGGGGCCTATGATGGAAAAATTAAAGTGTGGGATCTTGTGGCTGCTTTGGACCCCCGTGCTCCTGCAGGGACACT

1600 1610 1620 1630 1640 1650 1660 1670 1680 1690
CTGTCTACGGACCCTTGTGGAGCATTCCGGAAGAGTTTTTCGACTACAGTTTGATGAATTCCAGATTGTCAGTAGTTCACATGATGACACAATC

1700 1710 1720 1730 1740 1750 1760 1770 1780
CTCATCTGGGACTTCCTAAATGATCCAGCTGCCCAAGCTGAACCCCCCCGTTCCCCTTCTCGAACATACACCTACATCTCCAGATAAATAACCA

1790 1800 1810 1820 1830 1840 1850 1860 1870 1880
TACACTGACCTCATACTTGCCCAGGACCCATTAAAGTTGCGGTATTTAACGTATCTGCCAATACCAGGATGAGCAACAACAGTAACAATCAAAC

1890 1900 1910 1920 1930 1940 1950 1960 1970
TACTGCCCAGTTTCCCTGGACTAGCCGAGGAGCAGGGCTTTGAGACTCCTGTTGGGACACAGTTGGTCTGCAGTCGGCCCAGGACGGTCTACTC

1980 1990 2000 2010 2020 2030 2040 2050 2060
AGCACAACTGACTGCTTCAGTGCTGCTATCAGAAGATGTCTTCTATCAATTGTGAATGATTGGAACTTTTAAACCTCCCCTCCTCTCCTCCTTT

2070 2080 2090 2100 2110 2120 2130 2140 2150
CACCTCTGCACCTAGTTTTTTCCCATTGGTTCCAGACAAAGGTGACTTATAAATATATTTAGTGTTTTGCCAGAAAAAAAAAA
```

FIG. 3B

10045427.010202

```
          10        20        30        40        50        60
MERKDFETWLDNISVTFLSLTDLQKNETLDHLISLSGAVQLRHLSNNLETLLKRDFLKLL

          70        80        90       100       110       120
PLELSFYLLKWLDPQTLLTCCLVSKQWNKVISACTEVWQTACKNLGWQIDDSVQDALHWK

         130       140       150       160       170       180
KVYLKAILRMKQLEDHEAFETSSLIGHSARVYALYYKDGLLCTGSDDLSAKLWDVSTGQC

         190       200       210       220       230       240
VYGIQTHTCAAVKFDEQKLVTGSFDNTVACWEWSSGARTQHFRGHTGAVFSVDYNDELDI

         250       260       270       280       290       300
LVSGSADFTVKVWALSAGTCLNTLTGHTEWVTKVVLQKCKVKSLLHSPGDYILLSADKYE

         310       320       330       340       350       360
IKIWPIGREINCKCLKTLSVSEDRSICLQPRLHFDGKYIVCSSALGLYQWDFASYDILRV

         370       380       390       400       410       420
IKTPEIANLALLGFGDIFALLFDNRYLYIMDLRTESLISRWPLPEYRESKRGSSFLAGEH

PG
```

FIG. 4A

```
        10        20        30        40        50        60        70        80        90
ATGGAGAGAAAGGACTTTGAGACATGGCTTGATAACATTTCTGTTACATTTCTTTCTCTGACGGACTTGCAGAAAAATGAAACTCTGGATCACC

   100       110       120       130       140       150       160       170       180
TGATTAGTCTGAGTGGGGCAGTCCAGCTCAGGCATCTCTCCAATAACCTAGAGACTCTCCTCAAGCGGGACTTCCTCAAACTCCTTCCCCTGGA

190       200       210       220       230       240       250       260       270       280
GCTCAGTTTTTATTTGTTAAAATGGCTCGATCCTCAGACTTTACTCACATGCTGCCTCGTCTCTAAACAGTGGAATAAGGTGATAAGTGCCTGT

      290       300       310       320       330       340       350       360       370
ACAGAGGTGTGGCAGACTGCATGTAAAAATTTGGGCTGGCAGATAGATGATTCTGTTCAGGACGCTTTGCACTGGAAGAAGGTTTATTTGAAGG

  380       390       400       410       420       430       440       450       460       470
CTATTTTGAGAATGAAGCAACTGGAGGACCATGAAGCCTTTGAAACCTCGTCATTAATTGGACACAGTGCCAGAGTGTATGCACTTTACTACAA

        480       490       500       510       520       530       540       550       560
AGATGGACTTCTCTGTACAGGGTCAGATGACTTGTCTGCAAAGCTGTGGGATGTGAGCACAGGGCAGTGCGTTTATGGCATCCAGACCCACACT

   570       580       590       600       610       620       630       640       650
TGTGCAGCGGTGAAGTTTGATGAACAGAAGCTTGTGACAGGCTCCTTTGACAACACTGTGGCTTGCTGGGAATGGAGTTCCGGAGCCAGGACCC

660       670       680       690       700       710       720       730       740       750
AGCACTTTCGGGGGCACACGGGGGCGGTATTTAGCGTGGACTACAATGATGAACTGGATATCTTGGTGAGCGGCTCTGCAGACTTCACTGTGAA

      760       770       780       790       800       810       820       830       840
AGTATGGGCTTTATCTGCTGGGACATGCCTGAACACACTCACCGGGCACACGGAATGGGTCACCAAGGTAGTTTTGCAGAAGTGCAAAGTCAAG

  850       860       870       880       890       900       910       920       930       940
TCTCTCTTGCACAGTCCTGGAGACTACATCCTCTTAAGTGCAGACAAATATGAGATTAAGATTTGGCCAATTGGGAGAGAAATCAACTGTAAGT

        950       960       970       980       990      1000      1010      1020      1030
GCTTAAAGACATTGTCTGTCTCTGAGGATAGAAGTATCTGCCTGCAGCCAAGACTTCATTTTGATGGCAAATACATTGTCTGTAGTTCAGCACT

    1040      1050      1060      1070      1080      1090      1100      1110      1120
TGGTCTCTACCAGTGGGACTTTGCCAGTTATGATATTCTCAGGGTCATCAAGACTCCTGAGATAGCAAACTTGGCCTTGCTTGGCTTTGGAGAT

1130      1140      1150      1160      1170      1180      1190      1200      1210      1220
ATCTTTGCCCTGCTGTTTGACAACCGCTACCTGTACATCATGGACTTGCGGACAGAGAGCCTGATTAGTCGCTGGCCTCTGCCAGAGTACAGGG

      1230      1240      1250      1260      1270      1280      1290      1300      1310
AATCAAAGAGAGGCTCAAGCTTCCTGGCAGGCGAACATCCTGGCTGAATGGACTGGATGGGCACAATGACACGGGCTTGGTCTTTGCCACCAGC

1320      1330      1340      1350      1360      1370      1380      1390      1400      1410
ATGCCTGACCACAGTATTCACCTGGTGTTGTGGAAGGAGCACGGCTGACACCATGAGCCACCACCGCTGACTGACTTTGGGTGCCGGGGCTGCG

      1420      1430      1440      1450      1460      1470
GGTTTTGGGTGCACCTCTGCGGCACGCGACTGCATGAACCAAAGTTCTCACCTAATGGTATCATCA
```

FIG. 4B

```
          10         20         30         40         50         60
MKRGGRDSDRNSSEEGTAEKSKKLRTTNEHSQTCDWGNLLQDIILQVFKYLPLLDRAHAS

          70         80         90        100        110        120
QVCRNWNQVFHMPDLWRCFEFELNQPATSYLKATHPELIKQIIKRHSNHLQYVSFKVDSS

         130        140        150        160        170        180
KESAEAACDILSQLVNCSLKTLGLISTARPSFMDLPKSHFISALTVVFVNSKSLSSLKID

         190        200        210        220        230        240
DTPVDDPSLKVLVANNSDTLKLLKMSSCPHVSPAGILCVADQCHGLRELALNYHLLSDEL

         250        260        270        280        290        300
LLALSSEKHVRLEHLRIDVVSENPGQTHFHTIQKSSWDAFIRHSPKVNLVMYFFLYEEEF

         310        320        330        340        350        360
DPFFRYEIPATHLYFGRSVSKDVLGRVGMTCPRLVELVVCANGLRPLDEELIRIAERCKN

         370        380        390        400        410        420
LSAIGLGECEVSCSAFVEFVKMCGGRLSQLSIMEEVLIPDQKYSLEQIHWEVSKHLGRVW

FPDMMPTW
```

FIG. 5A

```
          10        20        30        40        50        60        70        80        90
CGGGGTGGTGTGTGGGGGAAGCCGCCCCCGGCAGCAGGATGAAACGAGGAGGAAGAGATAGTGACCGTAATTCATCAGAAGAAGGAACTGCAGA

    100       110       120       130       140       150       160       170       180
GAAATCCAAGAAACTGAGGACTACAAATGAGCATTCTCAGACTTGTGATTGGGGTAATCTCCTTCAGGACATTATTCTCCAAGTATTTAAATAT

190       200       210       220       230       240       250       260       270       280
TTGCCTCTTCTTGACCGGGCTCATGCTTCACAAGTTTGCCGCAACTGGAACCAGGTATTTCACATGCCTGACTTGTGGAGATGTTTTGAATTTG

      290       300       310       320       330       340       350       360       370
AACTGAATCAGCCAGCTACATCTTATTTGAAAGCTACCCATCCAGAGCTGATCAAACAGATTATTAAAAGACATTCAAACCATCTACAATATGT

  380       390       400       410       420       430       440       450       460       470
CAGCTTCAAGGTGGACAGCAGCAAGGAATCAGCTGAAGCAGCTTGTGATATACTATCGCAACTTGTGAATTGCTCTTTAAAAACACTTGGACTT

        480       490       500       510       520       530       540       550       560
ATTTCAACTGCTCGACCAAGCTTTATGGATTTACCAAAGTCTCACTTTATCTCTGCACTGACAGTTGTGTTCGTAAACTCCAAATCCCTGTCTT

    570       580       590       600       610       620       630       640       650
CGCTTAAGATAGATGATACTCCAGTAGATGATCCATCTCTCAAAGTACTAGTGGCCAACAATAGTGATACACTCAAGCTGTTGAAAATGAGCAG

660       670       680       690       700       710       720       730       740       750
CTGTCCTCATGTCTCTCCAGCAGGTATCCTTTGTGTGGCTGATCAGTGTCACGGCTTAAGAGAACTAGCCCTGAACTACCACTTATTGAGTGAT

      760       770       780       790       800       810       820       830       840
GAGTTGTTACTTGCATTGTCTTCTGAAAAACATGTTCGATTAGAACATTTGCGCATTGATGTAGTCAGTGAGAATCCTGGACAGACACACTTCC

  850       860       870       880       890       900       910       920       930       940
ATACTATTCAGAAGAGTAGCTGGGATGCTTTCATCAGACATTCACCCAAAGTGAACTTAGTGATGTATTTTTTTTTTATATGAAGAAGAATTTGA

        950       960       970       980       990      1000      1010      1020      1030
CCCCTTCTTTCGCTATGAAATACCTGCCACCCATCTGTACTTTGGGAGATCAGTAAGCAAAGATGTGCTTGGCCGTGTGGGAATGACATGCCCT

   1040      1050      1060      1070      1080      1090      1100      1110      1120
AGACTGGTTGAACTAGTAGTGTGTGCAAATGGATTACGGCCACTTGATGAAGAGTTAATTCGCATTGCAGAACGTTGCAAAAATTTGTCAGCTA

1130      1140      1150      1160      1170      1180      1190      1200      1210      1220
TTGGACTAGGGGAATGTGAAGTCTCATGTAGTGCCTTTGTTGAGTTTGTGAAGATGTGTGGTGGCCGCCTATCTCAATTATCCATTATGGAAGA

     1230      1240      1250      1260      1270      1280      1290      1300      1310
AGTACTAATTCCTGACCAAAAGTATAGTTTGGAGCAGATTCACTGGGAAGTGTCCAAGCATCTTGGTAGGGTGTGGTTTCCCGACATGATGCCC

1320      1330      1340      1350      1360      1370      1380      1390      1400
ACTTGGTAAAAACTGCATGATGAATAGCACCTTAATTTCAAGCAAATGTATTATAATTAAAGTTTTATTTGCTGTAAAAAAAAAAAAAAAA
```

FIG. 5B

```
              10         20         30         40         50         60
MKRNSLSVENKIVQLSGAAKQPKVGFYSSLNQTHTHTVLLDWGSLPHHVVLQIFQYLPLL

              70         80         90        100        110        120
DRACASSVCRRWNEVFHISDLWRKFEFELNQSATSSFKSTHPDLIQQIIKKHFAHLQYVS

             130        140        150        160        170        180
FKVDSSAESAEAACDILSQLVNCSIQTLGLISTAKPSFMNVSESHFVSALTVVFINSKSL

             190        200        210        220        230        240
SSIKIEDTPVDDPSLKILVANNSDTLRLPKMSSCPHVSSDGILCVADRCQGLRELALNYY

             250        260        270        280        290        300
ILTDELFLALSSETHVNLEHLRIDVVSENPGQIKFHAVKKHSWDALIKHSPRVNVVMHFF

             310        320        330        340        350        360
LYEEEFETFFKEETPVTHLYFGRSVSKVVLGRVGLNCPRLIELVVCANDLQPLDNELICI

             370        380        390        400        410        420
AEHCTNLTALGLSKCEVSCSAFIRFVRLCERRLTQLSVMEEVLIPDEDYSLDEIHTEVSK

             430
YLGRVWFPDVMPLW
```

FIG. 6A

```
           10        20        30        40        50        60
 ACATTTTCTAATGTTTACAGAATGAAGAGGAACAGTTTATCTGTTGAGAATAAAATTGTCCAGTTGTCA

70         80        90       100       110       120       130
 GGAGCAGCGAAACAGCCAAAAGTTGGGTTCTACTCTTCTCTCAACCAGACTCATACACACACGGTTCTT

140        150       160       170       180       190       200
 CTAGACTGGGGGAGTTTGCCTCACCATGTAGTATTACAAATTTTTCAGTATCTTCCTTTACTAGATCGG

 210       220       230       240       250       260       270
 GCCTGTGCATCTTCTGTATGTAGGAGGTGGAATGAAGTTTTTCATATTTCTGACCTTTGGAGAAAGTTT

  280       290       300       310       320       330       340
 GAATTTGAACTGAACCAGTCAGCTACTTCATCTTTTAAGTCCACTCATCCTGATCTCATTCAGCAGATC

   350       360       370       380       390       400       410
 ATTAAAAAGCATTTTGCTCATCTTCAGTATGTCAGCTTTAAGGTTGACAGTAGCGCTGAGTCAGCAGAA

    420       430       440       450       460       470       480
 GCTGCCTGTGATATACTCTCTCAGCTGGTAAATTGTTCCATCCAGACCTTGGGCTTGATTTCAACAGCC

     490       500       510       520       530       540       550
 AAGCCAAGTTTCATGAATGTGTCGGAGTCTCATTTTGTGTCAGCACTTACAGTTGTTTTTATCAACTCA

      560       570       580       590       600       610       620
 AAATCATTATCATCAATCAAAATTGAAGATACACCAGTGGATGATCCTTCATTGAAGATTCTTGTGGCC

       630       640       650       660       670       680       690
 AATAATAGTGACACTCTAAGACTCCCAAAGATGAGTAGCTGTCCTCATGTTTCATCTGATGGAATTCTT

        700       710       720       730       740       750
 TGTGTAGCTGACCGTTGTCAAGGCCTTAGAGAACTGGCGTTGAATTATTACATCCTAACTGATGAACTT

760        770       780       790       800       810       820
 TTCCTTGCACTCTCAAGCGAGACTCATGTTAACCTTGAACATCTTCGAATTGATGTTGTGAGTGAAAAT

 830       840       850       860       870       880       890
 CCTGGACAGATTAAATTTCATGCTGTTAAAAAACACAGTTGGGATGCACTTATTAAACATTCCCCTAGA

 900       910       920       930       940       950       960
 GTTAATGTTGTTATGCACTTCTTTCTATATGAAGAGGAATTCGAGACGTTCTTCAAAGAAGAAACCCCT

  970       980       990      1000      1010      1020      1030
 GTTACTCACCTTTATTTTGGTCGTTCAGTCAGCAAAGTGGTTTTAGGACGGGTAGGTCTCAACTGTCCT

  1040      1050      1060      1070      1080      1090      1100
 CGACTGATTGAGTTAGTGGTGTGTGCTAATGATCTTCAGCCTCTTGATAATGAACTTATTTGTATTGCT

   1110      1120      1130      1140      1150      1160      1170
 GAACACTGTACAAACCTAACAGCCTTGGGCCTCAGCAAATGTGAAGTTAGCTGCAGTGCCTTCATCAGG

    1180      1190      1200      1210      1220      1230      1240
 TTTGTAAGACTGTGTGAGAGAAGGTTAACACAGCTCTCTGTAATGGAGGAAGTTTTGATCCCTGATGAG

     1250      1260      1270      1280      1290      1300      1310
 GATTATAGCCTAGATGAAATTCACACTGAAGTCTCCAAATACCTGGGAAGAGTATGGTTCCCTGATGTG

      1320
 ATGCCTCTCTGG
```

FIG. 6B

```
         10        20        30        40        50        60
MAGSEPRSGTNSPPPPFSDWGRLEAAILSGWKTFWQSVSKDRVARTTSREEVDEAASTLT

         70        80        90       100       110       120
RLPIDVQLYILSFLSPHDLCQLGSTNHYWNETVRNPILWRYFLLRDLPSWSSVDWKSLPY

        130       140       150       160       170       180
LQILKKPISEVSDGAFFDYMAVYLMCCPYTRRASKSSRPMYGAVTSFLHSLIIPNEPRFA

        190       200       210       220       230       240
LFGPRLEQLNTSLVLSLLSSEELCPTAGLPQRQIDGIGSGVNFQLNNQHKFNILILYSTT

        250       260       270       280       290       300
RKERDRAREEHTSAVNKMFSRHNEGDDRPGSRYSVIPQIQKLCEVVDGFIYVANAEAHKR

        310       320       330       340       350       360
HEWQDEFSHIMAMTDPAFGSSGRPLLVLSCISQGDVKRMPCFYLAHELHLNLLNHPWLVQ

        370       380       390       400       410       420
DTEAETLTGFLNGIEWILEEVESKRAR*FSFQILGTETI*NLLLRS*CEYLLSQPTLSCL

        430       440       450       460       470       480
FADRLSFGQL*LLCFLYYFYFLP*INYKKRVSVLVFSPKMNL*TFFW*FLYFLSF*KY*I

L
```

FIG. 7A

```
          10         20         30         40         50         60
ATGGCGGGAAGCGAGCCGCGCAGCGGAACAAATTCGCCGCCGCCGCCCTTCAGCGACTGGGGCCGCCTG

70         80         90        100        110        120        130
 GAGGCGGCCATCCTCAGCGGCTGGAAGACCTTCTGGCAGTCAGTGAGCAAGGATAGGGTGGCGCGTACG

140        150        160        170        180        190        200
 ACCTCCCGGGAGGAGGTGGATGAGGCGGCCAGCACCCTGACGCGGCTGCCGATTGATGTACAGCTATAT

210        220        230        240        250        260        270
ATTTTGTCCTTTCTTTCACCTCATGATCTGTGTCAGTTGGGAAGTACAAATCATTATTGGAATGAAACT

 280        290        300        310        320        330        340
GTAAGAAATCCAATTCTGTGGAGATACTTTTTGTTGAGGGATCTTCCTTCTTGGTCTTCTGTTGACTGG

  350        360        370        380        390        400        410
AAGTCTCTTCCATATCTACAAATCTTAAAAAAGCCTATATCTGAGGTCTCTGATGGTGCATTTTTTGAC

   420        430        440        450        460        470        480
TACATGGCAGTCTATCTAATGTGCTGTCCATACACAAGAAGAGCTTCAAAATCCAGCCGTCCTATGTAT

    490        500        510        520        530        540        550
GGAGCTGTCACTTCTTTTTTACACTCCCTGATCATTCCCAATGAACCTCGATTTGCTCTGTTTGGACCA

     560        570        580        590        600        610        620
CGTTTGGAACAATTGAATACCTCTTTGGTGTTGAGCTTGCTGTCTTCAGAGGAACTTTGCCCAACAGCT

      630        640        650        660        670        680        690
GGTTTGCCTCAGAGGCAGATTGATGGTATTGGATCAGGAGTCAATTTTCAGTTGAACAACCAACATAAA

       700        710        720        730        740        750
TTCAACATTCTAATCTTATATTCAACTACCAGAAAGGAAAGAGATAGAGCAAGGGAAGAGCATACAAGT

760        770        780        790        800        810        820
 GCAGTTAACAAGATGTTCAGTCGACACAATGAAGGTGATGATCGACCAGGAAGCCGGTACAGTGTGATT

830        840        850        860        870        880        890
 CCACAGATTCAAAAACTGTGTGAAGTTGTAGATGGGTTCATCTATGTTGCAAATGCTGAAGCTCATAAA

900        910        920        930        940        950        960
AGACATGAATGGCAAGATGAATTTTCTCATATTATGGCAATGACAGATCCAGCCTTTGGGTCTTCGGGA

 970        980        990       1000       1010       1020       1030
AGACCATTGTTGGTTTTATCTTGTATTTCTCAAGGGGATGTAAAAAGAATGCCCTGTTTTTATTTGGCT

 1040       1050       1060       1070       1080       1090       1100
CATGAGCTGCATCTGAATCTTCTAAATCACCCATGGCTGGTCCAGGATACAGAGGCTGAAACTCTGACT

  1110       1120       1130       1140       1150       1160       1170
GGTTTTTTGAATGGCATTGAGTGGATTCTTGAAGAAGTGGAATCTAAGCGTGCAAGATGATTCTCTTTT

   1180       1190       1200       1210       1220       1230       1240
CAGATCTTGGGAACTGAAACCATTTGAAATTTATTACTAAGGTCGTGATGTGAATATTTGCTCAGTCAG

    1250       1260       1270       1280       1290       1300       1310
CCCACCTTGTCCTGCCTTTTTGCAGATAGGCTTTCATTTGGACAGCTATAACTGCTGTGTTTTTTATAT

     1320       1330       1340       1350       1360       1370       1380
TATTTTTACTTTTTACCATAAATCAATTACAAGAAAAGAGTTTCAGTCCTAGTATTTAGCCCCAAAATG

      1390       1400       1410       1420       1430       1440
AACCTTTAAACATTTTTTTGGTAATTTTTATATTTTCTGTCTTTTTAAAAATATTAAATTTTGG
```

FIG. 7B

```
         10        20        30        40        50        60
MSRRPCSCALRPPRCSCSASPSAVTAAGRPRPSDSCKEESSTLSVKMKCDFNCNHVHSGL

         70        80        90       100       110       120
KLVKPDDIGRLVSYTPAYLEGSCKDCIKDYERLSCIGSPIVSPRIVQLETESKRLHNKEN

        130       140       150       160       170       180
QHVQQTLNSTNEIEALETSRLYEDSGYSSFSLQSGLSEHEEGSLLEENFGDSLQSCLLQI

        190       200       210       220       230       240
QSPDQYPNKNLLPVLHFEKVVCSTLKKNAKRNPKVDREMLKEIIARGNFRLQNIIGRKMG

        250       260       270       280       290       300
LECVDILSELFRRGLRHVLATILAQLSDMDLINVSKVSTTWKKILEDDKGAFQLYSKAIQ

        310       320       330       340       350       360
RVTENNNKFSPHASTREYVMFRTPLASVQKSAAQTSLKKDAQTKLSNQGDQKGSTYSRHN

        370       380       390       400       410       420
EFSEVAKTLKKNESLKACIRCNSPAKYDCYLQRATCKREGCGFDYCTKCLCNYHTTKDCS

        430       440
DGKLLKASCKIGPLPGTKKSKKNLRRL
```

FIG. 8A

```
         10        20        30        40        50        60        70        80        90
AGGTTGCTCAGCTGCCCCCGGAGCGGTTCCTCCACCTGAGGCAGACACCACCTCGGTTGGCATGAGCCGGCGCCCCTGCAGCTGCGCCCTACGG

   100       110       120       130       140       150       160       170       180
CCACCCCGCTGCTCCTGCAGCGCCAGCCCCAGCGCAGTGACAGCCGCCGGGCGCCCTCGACCCTCGGATAGTTGTAAAGAAGAAAGTTCTACCC

190       200       210       220       230       240       250       260       270       280
TTTCTGTCAAAATGAAGTGTGATTTTAATTGTAACCATGTTCATTCCGGACTTAAACTGGTAAAACCTGATGACATTGGAAGACTAGTTTCCTA

     290       300       310       320       330       340       350       360       370
CACCCCTGCATATCTGGAAGGTTCCTGTAAAGACTGCATTAAAGACTATGAAAGGCTGTCATGTATTGGGTCACCGATTGTGAGCCCTAGGATT

 380       390       400       410       420       430       440       450       460       470
GTACAACTTGAAACTGAAAGCAAGCGCTTGCATAACAAGGAAAATCAACATGTGCAACAGACACTTAATAGTACAAATGAAATAGAAGCACTAG

       480       490       500       510       520       530       540       550       560
AGACCAGTAGACTTTATGAAGACAGTGGCTATTCCTCATTTTCTCTACAAAGTGGCCTCAGTGAACATGAAGAAGGTAGCCTCCTGGAGGAGAA

   570       580       590       600       610       620       630       640       650
TTTCGGTGACAGTCTACAATCCTGCCTGCTACAAATACAAAGCCCAGACCAATATCCCAACAAAAACTTGCTGCCAGTTCTTCATTTTGAAAAA

660       670       680       690       700       710       720       730       740       750
GTGGTTTGTTCAACATTAAAAAAGAATGCAAAACGAAATCCTAAAGTAGATCGGGAGATGCTGAAGGAAATTATAGCCAGAGGAAATTTTAGAC

     760       770       780       790       800       810       820       830       840
TGCAGAATATAATTGGCAGAAAAATGGGCCTAGAATGTGTAGATATTCTCAGCGAACTCTTTCGAAGGGGACTCAGACATGTCTTAGCAACTAT

 850       860       870       880       890       900       910       920       930       940
TTTAGCACAACTCAGTGACATGGACTTAATCAATGTGTCTAAAGTGAGCACAACTTGGAAGAAGATCCTAGAAGATGATAAGGGGGCATTCCAG

       950       960       970       980       990      1000      1010      1020      1030
TTGTACAGTAAAGCAATACAAAGAGTTACCGAAAACAACAATAAATTTTCACCTCATGCTTCAACCAGAGAATATGTTATGTTCAGAACCCCAC

 1040      1050      1060      1070      1080      1090      1100      1110      1120
TGGCTTCTGTTCAGAAATCAGCAGCCCAGACTTCTCTCAAAAAAGATGCTCAAACCAAGTTATCCAATCAAGGTGATCAGAAAGGTTCTACTTA

1130      1140      1150      1160      1170      1180      1190      1200      1210      1220
TAGTCGACACAATGAATTCTCTGAGGTTGCCAAGACATTGAAAAAGAACGAAAGCCTCAAAGCCTGTATTCGCTGTAATTCACCTGCAAAATAT

    1230      1240      1250      1260      1270      1280      1290      1300      1310
GATTGCTATTTACAACGGGCAACCTGCAAACGAGAAGGCTGTGGATTTGATTATTGTACGAAGTGTCTCTGTAATTATCATACTACTAAAGACT

1320      1330      1340      1350      1360      1370      1380      1390      1400      1410
GTTCAGATGGCAAGCTCCTCAAAGCCAGTTGTAAAATAGGTCCCCTGCCTGGTACAAAGAAAAGCAAAAAGAATTTACGAAGATTGTGATCTCT

      1420      1430      1440      1450      1460      1470      1480      1490      1500
TATTAAATCAATTGTTACTGATCATGAATGTTAGTTAGAAAATGTTAGGTTTTAACTTAAAAAAAATTGTATTGTGATTTTCAATTTTATGTTG

  1510      1520      1530      1540      1550      1560      1570      1580      1590
AAATCGGTGTAGTATCCTGAGGTTTTTTTCCCCCCAGAAGATAAAGAGGATAGACAACCTCTTAAAATATTTTTACAATTTAATGAGAAAAAGT

1600      1610      1620      1630      1640      1650      1660      1670      1680      1690
TTAAAATTCTCAATACAAATCAAACAATTTAAATATTTTAAGAAAAAAGGAAAAGTAGATAGTGATACTGAGGGTAAAAAAAAAATTGATTCAA

    1700      1710      1720      1730      1740      1750      1760      1770      1780
TTTTATGGTAAAGGAAACCCATGCAATTTTACCTAGACAGTCTTAAATATGTCTGGTTTTCCATCTGTTAGCATTTCAGACATTTTATGTTCCT

1790      1800      1810      1820      1830      1840      1850      1860      1870      1880
CTTACTCAATTGATACCAACAGAAATATCAACTTCTGGAGTCTATTAAATGTGTTGTCACCTTTCTAAAGCTTTTTTTCATTGTGTGTATTTCC

      1890      1900      1910      1920      1930      1940      1950      1960      1970
CAAGAAAGTATCCTTTGTAAAAACTTGCTTGTTTTCCTTATTTCTGAAATCTGTTTTAATATTTTTGTATACATGTAAATATTTCTGTATTTTT

  1980      1990      2000      2010      2020      2030      2040      2050      2060
TATATGTCAAAGAATATGTCTCTTGTATGTACATATAAAAATAAATTTTGCTCAATAAAATTGTAAGCTTAAAAAAAAAAAAAAAAAAACTCGAG

2070
ACTAGTGC
```

FIG. 8B

```
             10        20        30        40        50        60
ARSGASALRRRRVQVWVLSRPPPGGGDSFRTRRPQRGPGPGGSQAMDAPHSKAALDSINE

             70        80        90       100       110       120
LPDNILLELFTHVPARQLLLNCRLVCSLWRDLIDLLTLWKRKCLRKGFITKDWDQPVADW

            130       140       150       160       170       180
KIFYFLRSLHRNLLRNPCAENDMFAWQIDFNGGDRWKVDSLPGAHGTEFPDPKVKKSFVT

            190       200       210       220       230       240
SYELCLKWELVDLLADRYWEELLDTFRPDIVVKDWFAARADCGCTYQLKVQLASADYFVL

            250       260       270       280       290       300
ASFEPPPVTIQQWNNATWTEVSYTFSDYPRGVRYILFQHGGRDTQYWAGWYGPRVTNSSI

            310       320       330
VVSPKMTRNQASSEAQPGQKHGQEEAAQSPYGAVVQIF
```

FIG. 9A

```
        10        20        30        40        50        60        70        80        90
GCGCGTTCGGGAGCTTCGGCCCTGCGTAGGAGGCGGGTGCAGGTGTGGGTGCTGAGCCGCCCGCCGCCTGGAGGGGGAGACAGCTTCAGGACAC

     100       110       120       130       140       150       160       170       180
GCAGGCCGCAGCGAGGGCCCGGGCCCGGGGGATCCCAGGCCATGGACGCTCCCCACTCCAAAGCAGCCCTGGACAGCATTAACGAGCTGCCCGA

190       200       210       220       230       240       250       260       270       280
TAACATCCTGCTGGAGCTGTTCACGCACGTGCCCGCCCGCCAGCTGCTGCTGAACTGCCGCCTGGTCTGCAGCCTCTGGCGGGACCTCATCGAC

      290       300       310       320       330       340       350       360       370
CTCCTGACCCTCTGGAAACGCAAGTGCCTGCGAAAGGGCTTCATCACCAAGGACTGGGACCAGCCCGTGGCCGACTGGAAAATCTTCTACTTCC

  380       390       400       410       420       430       440       450       460       470
TACGGAGCCTGCATAGGAACCTCCTGCGCAACCCGTGTGCTGAAAACGATATGTTTGCATGGCAAATTGATTTCAATGGTGGGGACCGCTGGAA

       480       490       500       510       520       530       540       550       560
GGTGGATAGCCTCCCTGGAGCCCACGGGACAGAATTTCCTGACCCCAAAGTCAAGAAGTCTTTTGTCACATCCTACGAACTGTGCCTCAAGTGG

     570       580       590       600       610       620       630       640       650
GAGCTGGTGGACCTTCTAGCCGACCGCTACTGGGAGGAGCTACTAGACACATTCCGGCCGGACATCGTGGTTAAGGACTGGTTTGCTGCCAGAG

660       670       680       690       700       710       720       730       740       750
CCGACTGTGGCTGCACCTACCAACTCAAAGTGCAGCTGGCCTCGGCTGACTACTTCGTGTTGGCCTCCTTCGAGCCCCCACCTGTGACCATCCA

      760       770       780       790       800       810       820       830       840
ACAGTGGAACAATGCCACATGGACAGAGGTCTCCTACACCTTCTCAGACTACCCCCGGGGTGTCCGCTACATCCTCTTCCAGCATGGGGGCAGG

  850       860       870       880       890       900       910       920       930       940
GACACCCAGTACTGGGCAGGCTGGTATGGGCCCCGAGTCACCAACAGCAGCATTGTCGTCAGCCCCAAGATGACCAGGAACCAGGCCTCGTCCG

        950       960       970       980       990      1000      1010      1020      1030
AGGCTCAGCCTGGGCAGAAGCATGGACAGGAGGAGGCTGCCCAATCGCCCTACGGAGCTGTTGTCCAGATTTTCTGACAGCTGTCCATCCTGTG

   1040      1050      1060      1070      1080      1090      1100      1110      1120
TCTGGGTCAGCCAGAGGTTCCTCCAGGCAGGAGCTGAGCATGGGGTGGCAGTGAGGTCCCTGTACCAGCGACTCCTGCCCCGGTTCAACCCTA

1130      1140      1150      1160      1170      1180      1190      1200      1210      1220
CCAGCTTGTGGTAACTTACTGTCACATAGCTCTGACGTTTTGTTGTAATAAATGTTTTCAGGCCGGGCACTGTGGCTCACGCCTGTAATCCCAG

    1230      1240      1250      1260      1270      1280      1290      1300      1310
CACTTTGGGAGACCGAGGCAGGTGGATCACGAGGTCAGGAGACAGAGACCATCCTGGCCAACACGGTGAAACCCTGTCTCTACTAAAAATACAA

1320      1330      1340      1350      1360      1370      1380      1390      1400      1410
AAAATTAGCCGGGCGTGGTGGCGGGCGCCTGTAGTCCCAGCTACTCGGGAGGCTGATGCAGAAGAATGGCGTGAACCCGGAAGGCAGAGCTTGC

      1420      1430      1440      1450      1460      1470      1480      1490      1500
AGTGAGCCGAGATCACGCCACTGCACTCCAGCCTGGGTGACAGAGCGAGACTCTGGCTCATAAAATAATAATAATAATAAATAAATAAAAAATA

 1510      1520      1530
AATGGTTTTCAGTAAAAAAAAAAAAAAAAAA
```

FIG. 9B

```
         10        20        30        40        50        60
MSNTRFTITLNYKDPLTGDEETLASYGIVSGDLICLILHDDIPPPNIPSSTDSEHSSLQN

         70        80        90       100       110       120
NEQPSLATSSNQTSIQDEQPSDSFQGQAAQSGVWNDDSMLGPSQNFEAESIQDNAHMAEG

        130       140       150       160       170       180
TGFYPSEPLLCSESVEGQVPHSLETLYQSADCSDANDALIVLIHLLMLESGYIPQGTEAK

        190       200       210       220       230       240
ALSLPEKWKLSGVYKLQYMHHLCEGSSATLTCVPLGNLIVVNATLKINNEIRSVKRLQLL

        250       260       270       280       290       300
PESFICKEKLGENVANIYKDLQKLSRLFKDQLVYPLLAFTRQALNLPNVFGLVVLPLELK

        310       320       330       340       350       360
LRIFRLLDVRSVLSLSAVCRDLFTASNDPLLWRFLYLRDFRDNTVRVQDTDWKELYRKRH

        370       380       390       400       410       420
IQRKESPKGRFVLLLPSSTHTIPFYPNPLHPRPFPSSRLPPGIIGGEYDQRPTLPYVGDP

        430       440       450       460       470       480
ISSLIPGPGETPSQLPPLRPRFDPVGPLPGPNPILPGRGGPNDRFPFRPSRGRPTDGRLS

FM
```

FIG. 10A

```
      10         20         30         40         50         60         70         80         90
TGGAATTCCCATGGACCATGTCTAATACCCGATTTACAATTACATTGAACTACAAGGATCCCCTCACTGGAGATGAAGAGACCTTGGCTTCATA

  100        110        120        130        140        150        160        170        180
TGGGATTGTTTCTGGGGACTTGATATGTTTGATTCTTCACGATGACATTCCACCGCCTAATATACCTTCATCCACAGATTCAGAGCATTCTTCA

190        200        210        220        230        240        250        260        270        280
CTCCAGAACAATGAGCAACCCTCTTTGGCCACCAGCTCCAATCAGACTAGCATACAGGATGAACAACCAAGTGATTCATTCCAAGGACAGGCAG

    290        300        310        320        330        340        350        360        370
CCCAGTCTGGTGTTTGGAATGACGACAGTATGTTAGGGCCTAGTCAAAATTTTGAAGCTGAGTCAATTCAAGATAATGCGCATATGGCAGAGGG

 380        390        400        410        420        430        440        450        460        470
CACAGGTTTCTATCCCTCAGAACCCCTGCTCTGTAGTGAATCGGTGGAAGGGCAAGTGCCACATTCATTAGAGACCTTGTATCAATCAGCTGAC

     480        490        500        510        520        530        540        550        560
TGTTCTGATGCCAATGATGCGTTGATAGTGTTGATACATCTTCTCATGTTGGAGTCAGGTTACATACCTCAGGGCACCGAAGCCAAAGCACTGT

   570        580        590        600        610        620        630        640        650
CCCTGCCGGAGAAGTGGAAGTTGAGCGGGGTGTATAAGCTGCAGTACATGCATCATCTCTGCGAGGGCAGCTCCGCTACTCTCACCTGTGTGCC

660        670        680        690        700        710        720        730        740        750
TTTGGGAAACCTGATTGTTGTAAATGCTACACTAAAAATCAACAATGAGATTAGAAGTGTGAAAAGATTGCAGCTGCTACCAGAATCTTTTATT

    760        770        780        790        800        810        820        830        840
TGCAAAGAGAAACTAGGGGAAAATGTAGCCAACATATACAAAGATCTTCAGAAACTCTCTCGCCTCTTTAAAGACCAGCTGGTGTATCCTCTTC

 850        860        870        880        890        900        910        920        930        940
TGGCTTTTACCCGACAAGCACTGAACCTACCAAATGTATTTGGGTTGGTCGTCCTCCCATTGGAACTGAAACTACGGATCTTCCGACTTCTGGA

     950        960        970        980        990        1000       1010       1020       1030
TGTTCGTTCCGTCTTGTCTTTGTCTGCGGTTTGTCGTGACCTCTTTACTGCTTCAAATGACCCACTCCTGTGGAGGTTTTTATATCTGCGTGAT

  1040       1050       1060       1070       1080       1090       1100       1110       1120
TTTCGAGACAATACTGTCAGAGTTCAAGACACAGATTGGAAAGAACTGTACAGGAAGAGGCACATACAAAGAAAAGAATCCCCGAAAGGGCGGT

1130       1140       1150       1160       1170       1180       1190       1200       1210       1220
TTGTGCTGCTCCTGCCATCGTCAACCCACACCATTCCATTCTATCCCAACCCCTTGCACCCTAGGCCATTTCCTAGCTCCCGCCTTCCTCCAGG

    1230       1240       1250       1260       1270       1280       1290       1300       1310
AATTATCGGGGGTGAATATGACCAAAGACCAACACTTCCCTATGTTGGAGACCCAATCAGTTCACTCATTCCTGGTCCTGGGGAGACGCCCAGC

1320       1330       1340       1350       1360       1370       1380       1390       1400       1410
CAGTTACCTCCACTGAGACCACGCTTTGATCCAGTTGGCCCACTTCCAGGACCTAACCCCATCTTGCCAGGGCGAGGCGGCCCCAATGACAGAT

    1420       1430       1440       1450       1460       1470       1480       1490       1500
TTCCCTTTAGACCCAGCAGGGGTCGGCCAACTGATGGCCGCCTGTCATTCATGTGATTGATTTGTAATTTCATTTCTGGAGCTCCATTTGTTTT

 1510       1520       1530       1540       1550       1560       1570       1580       1590
TGTTTCTAAACTACAGATGTCACTCCTTGGGGTGCTGATCTCGAGTGTTATTTTCTGATTGTGGTGTTGAGAGTTGCACTCCCAGAAACCTTTT

1600       1610       1620       1630       1640       1650       1660       1670       1680       1690
AAGAGATACATTTATAGCCCTAGGGGTGGTATGACCCAAAGGTTCCTCTGTGACAAGGTTGGCCTTGGGAATAGTTGGCTGCCAATCTCCCTGC

    1700       1710       1720       1730       1740       1750       1760
TCTTGGTTCTCCTCTAGATTGAAGTTTGTTTTCTGATGCTGTTCTTACCAGATTAAAAAAAAGTGTAAATT
```

FIG. 10B

```
        10        20        30        40        50        60
ETSKLG*SAVLAPAAGGTLSSEGRSAVSGILIAVTSTGVDK*SLNQLLHGLGTSSRLSHF

        70        80        90       100       110       120
PFG*KSPPRGQFVAAAVEIAGRSGLQMGQGLWRVVRNQQLQQEGYSEQGYLTREQSRRMA

       130       140       150       160       170       180
ASNISNTNHRKQVQGGIDIYHLLKARKSKEQEGFINLEMLPPELSFTILSYLNATDLCLA

       190       200       210       220       230       240
SCVWQDLANDELLWQGLCKSTWGHCSIYNKNPPLGFSFRKXYMQLDEGSLTFNANPDEGV

       250       260       270       280       290       300
NYFMSKGILDDSPKEIAKFIFCTRTLNWKKLRIYLDERRDVLDDLVTLHNFRNQFLPNAL

       310       320       330       340       350       360
REFFRHIHAPEERGEYLETLITKFSHRFCACNPDLMRELGLSPDAVYVLCYSLILLSIDL

       370       380       390       400       410       420
TSPHVKNKMSKREFIRNTRRAAQNISEDFVGHLYDNIYLIGHVAA*KAQLLGLQFLLQTK

       430       440       450       460       470       480
ATQGLSRYGGYISAGHCSLSIQSSFSVQPFFLLPFSILVISLGN*IILQNFS*FCLSRFA

       490       500       510       520       530       540
QSRATV*HSC*RMIN*HYTLKDGVFVH*ICLKNFIHFHSLYKYHVMCTYLTKEIYSHNYF

       550       560       570       580       590       600
IVKILTKVFPFLSN*VLKFI*F*SETIVXVKVRSDFRQKPIPASFSFKL*RVLICYYITM

       610       620       630       640       650
QNWQLFL*YKFII*FFILKTGLIKSR*VL*TI*DF*NIKIYDLHS*E*NKIXLELW
```

FIG. 11A

```
        10        20        30        40        50        60        70        80        90
GGAAACGTCAAAATTGGGATAGTCGGCAGTTCTGGCCCCTGCAGCTGGAGGTACCCTGAGTTCTGAGGGTCGTAGTGCTGTTTCTGGTATTCTC

     100       110       120       130       140       150       160       170       180
ATCGCGGTCACCTCTACCGGTGTGGACAAGTAAAGTTTGAATCAGCTTCTCCATGGCCTGGGCACCAGTTCCCGGCTGAGCCATTTTCCTTTTG

190       200       210       220       230       240       250       260       270       280
GCTAAAAGTCCCCGCCCAGAGGCCAATTCGTCGCGGCGGCGGTGGAGATCGCAGGTCGCTCAGGCTTGCAGATGGGTCAAGGGTTGTGGAGAGT

      290       300       310       320       330       340       350       360       370
GGTCAGAAACCAGCAGCTGCAACAAGAAGGCTACAGTGAGCAAGGCTACCTCACCAGAGAGCAGAGCAGGAGAATGGCTGCGAGCAACATTTCT

 380       390       400       410       420       430       440       450       460       470
AACACCAATCATCGTAAACAAGTCCAAGGAGGCATTGACATATATCATCTTTTGAAGGCAAGGAAATCGAAAGAACAGGAAGGATTCATTAATT

       480       490       500       510       520       530       540       550       560
TGGAAATGTTGCCTCCTGAGCTAAGCTTTACCATCTTGTCCTACCTGAATGCAACTGACCTTTGCTTGGCTTCATGTGTTTGGCAGGACCTTGC

   570       580       590       600       610       620       630       640       650
GAATGATGAACTTCTCTGGCAAGGGTTGTGCAAATCCACTTGGGGTCACTGTTCCATATACAATAAGAACCCACCTTTAGGATTTTCTTTTAGA

660       670       680       690       700       710       720       730       740       750
AAAKTGTATATGCAGCTGGATGAAGGCAGCCTCACCTTTAATGCCAACCCAGATGAGGGAGTGAACTACTTTATGTCCAAGGGTATCCTGGATG

      760       770       780       790       800       810       820       830       840
ATTCGCCAAAGGAAATAGCAAAGTTTATCTTCTGTACAAGAACACTAAATTGGAAAAAACTGAGAATCTATCTTGATGAAAGGAGAGATGTCTT

 850       860       870       880       890       900       910       920       930       940
GGATGACCTTGTAACATTGCATAATTTTAGAAATCAGTTCTTGCCAAATGCACTGAGAGAATTTTTTCGTCATATCCATGCCCCTGAAGAGCGT

       950       960       970       980       990      1000      1010      1020      1030
GGAGAGTATCTTGAAACTCTTATAACAAAGTTCTCACATAGATTCTGTGCTTGCAACCCTGATTTAATGCGAGAACTTGGCCTTAGTCCTGATG

  1040      1050      1060      1070      1080      1090      1100      1110      1120
CTGTCTATGTACTGTGCTACTCTTTGATTCTACTTTCCATTGACCTCACTAGCCCTCATGTGAAGAATAAAATGTCAAAAAGGGAATTTATTCG

1130      1140      1150      1160      1170      1180      1190      1200      1210      1220
AAATACCCGTCGCGCTGCTCAAAATATTAGTGAAGATTTTGTAGGGCATCTTTATGACAATATCTACCTTATTGGCCATGTGGCTGCATAAAAA

      1230      1240      1250      1260      1270      1280      1290      1300      1310
GCACAATTGCTAGGACTTCAGTTTTTACTTCAGACTAAAGCTACCCAAGGACTTAGCAGATATGGGGGTTACATCAGTGCTGGTCATTGTAGCC

1320      1330      1340      1350      1360      1370      1380      1390      1400      1410
TGAGTATACAATCAAGCTTCAGTGTGCAACCTTTTTTTCTTTTGCCATTTTCTATTTTAGTAATTTCCTTGGGGAACTAAATAATTTTGCAGAA

      1420      1430      1440      1450      1460      1470      1480      1490      1500
TTTTTCCTAATTTTGTTTATCACGTTTTGCACAAAGCAGAGCCACTGTCTAACACAGCTGTTAACGAATGATAAACTGACATTATACTCTAAAA

  1510      1520      1530      1540      1550      1560      1570      1580      1590
GATGGTGTATTTGTGCATTAGATTTGCCTGAAAAACTTTATCCATTTCCATTCTTTATACAAATACCATGTAATGTGTACATATTTAACTAAAG

1600      1610      1620      1630      1640      1650      1660      1670      1680      1690
AGATTTATAGTCATAATTATTTTATTGTAAAGATTTTAACTAAAGTTTTTCCTTTTCTCTCAAACTGAGTTCTGAAATTTATTTGATTCTGATC

      1700      1710      1720      1730      1740      1750      1760      1770      1780
TGAAACTATTGTCTYCGTAAAAGTTAGATCTGACTTCAGRCAGAAACCAATACCAGCTTCCTTTTCCTTTAAACTTTGAAGAGTGTTGATTTGT

1790      1800      1810      1820      1830      1840      1850      1860      1870      1880
TACTATATTACTATGCAAAACTGGCAGTTATTTTTATAATATAAATTTATAATTTGATTTTTTATTTTAAAAACTGGGTTAATCAAGTCTCGGT

      1890      1900      1910      1920      1930      1940      1950      1960      1970
AAGTCCTTTAAACCATTTAGGATTTTTAAAACATCAAAATTTATGATTTACATTCATAGGAATAAAATAAAATATYATTAGAACTCTGGT
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FIG. 11B

```
          10        20        30        40        50        60
MAAAAVDSAMEVVPALAEEAAPEVAGLSCLVNLPGEVLEYILCCGSLTAADIGRVSSTCR

          70        80        90       100       110       120
RLRELCQSSGKVWKEQFRVRWPSLMKHYSPTDYVNWLEEYKVRQKAGLEARKIVASFSKR

         130       140       150       160       170       180
FFSEHVPCNGFSDIENLEGPEIFFEDELVCILNMEGRKALTWKYYAKKILYYLRQQKILN

         190       200       210       220       230       240
NLKAFLQQPDDYESYLEGAVYIDQYCNPLSDISLKDIQAQIDSIVELVCKTLRGINSRHP

         250       260       270       280       290       300
SLAFKAGESSMIMEIELQSQVLDAMNYVLYDQLKFKGNRMDYYNALNLYMHQVLIRRTGI

         310       320       330       340       350       360
PISMSLLYLTIARQLGVPLEPVNFPSHFLLRWCQGAEGATLDIFDYIYIDAFGKGKQLTV

         370       380       390       400       410       420
KECEYLIGQHVTAALYGVVNVKKVLQRMVGNLLSLGKREGIDQSYQLLRDSLDLYLAMYP

         430       440       450       460       470       480
DQVQLLLLQARLYFHLGIWPEKVLDILQHIQTLDPGQHGAVGYLVQHTLEHIERKKEEVG

         490       500       510       520       530       540
VEVKLRSDEKHRDVCYSIGLIMKHKRYGYNCVIYGWDPTCMMGHEWIRNMNVHSLPHGHH

         550       560       570       580       590       600
QPFYNVLVEDGSCRYAAQENLEYNVEPQEISHPDVGRYFSEFTGTHYIPNAELEIRYPED

         610       620
LEFVYETVQNIYSAKKENIDE
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FIG. 12A

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          10        20        30        40        50        60        70        80        90       100       110       120       130
GATGGCGGCGGCAGCAGTCGACAGCCCGATGGAGGTGGTGCCGGCGCTGGCCGAGGAGGCCGCGCCCGAGGTAGCGGGCCTCAGCTGCCTCGTCAACCTGCCCGGTGAGGTGCTGGAGTACATCCTGTGCTGCGGCTCG
140       150       160       170       180       190       200       210       220       230       240       250       260       270
CTGACGGCCGCCCGACATCGGCCGTGTCTCCAGCACCTGCCGGCGGCTGCGCGAGCTGTGCCAGAGCAGCGGGAAGGTGTGGAAGGAGCAGTTCCGGGTGAGGTGGCCTTCCCTTATGAAACACTACAGCCCCACCGACT
280       290       300       310       320       330       340       350       360       370       380       390       400       410
ACGTCAATTGGTTGGAAGAGTATAAAGTTCGGCAAAAAGCTGGGTTAGAAGCGGGAAGATTGTAGCCTCGTTCTCAAAGAGGTTCTTTTCAGAGCACGTTCCTTGTAATGGCTTCAGTGACATTGAGAACCTTGAAGG
420       430       440       450       460       470       480       490       500       510       520       530       540       550
ACCAGAGATTTTTTTTGAGGATGAACTGGTGTGTATCCTAAATATGGAAGGAAGAAAAGCTTTGACCTGGAAATACTACGCAAAAAAAAATTCTTTACTACCTGCGGCAACAGAAGATCTTAAATAATCTTAAGCCTTT
560       570       580       590       600       610       620       630       640       650       660       670       680       690
CTTCAGCCAGCCAGATGACTATGAGTCGTATCTTGAAGGTGCTGTATATATTGACCAGTACTGCAATCCTCTCTCCGACATCAGCCTCAAAGACATCCAGGCCCAAATTGACAGCATCGTGGAGCTTGTTTGCAAAACCC
700       710       720       730       740       750       760       770       780       790       800       810       820       830
TTCGGGGCATAAACAGTCGCCACCCCAGCTTGGCCTTCAAGGCAGGTGAATCATCCATGATAATGGAAATAGAACTCCAGAGCCAGGTGCTGGATGCCATGAACTATGTCCTTTACGACCAACTGAAGTTCAAGGGAA
840       850       860       870       880       890       900       910       920       930       940       950       960       970
TCGAATGGATTACTATAATGCCCTCAACTTATATATGCATCAGGTTTTGATTCGCAGAACAGGAATCCCAATCAGCATGTCTCTGCTCTATTTGACAATTGCTCGGCAGTTGGGAGTCCCACTGGAGCCTGTCAACTTC
980       990      1000      1010      1020      1030      1040      1050      1060      1070      1080      1090      1100      1110
CCAAGTCACTTCTTATTAAGGTGGTGCCAAGGCGCAGAAGGGGCGACCCTGGACATCTTTGACTACATCTACATAGATGCTTTTGGAAAGGCAAGCAGCTGACAGTGAAAGAATGCGAGTACTTGATCGGCCAGCACG
1120      1130      1140      1150      1160      1170      1180      1190      1200      1210      1220      1230      1240      1250
TGACTGCAGCACTGTATGGGGTGGTCAATGTCAAGAAGGTGTTACAGAGAATGGTGGAAACCTGTTAAGCCTGGGGAAGCGGGAAGGCATCGACCAGTCATACCAGCTCCTGAGAGACTCGCTGGATCTCTATCTGGC
1260      1270      1280      1290      1300      1310      1320      1330      1340      1350      1360      1370      1380      1390
AATGTACCCGGACCAGGTGCAGCTTCTCCTCCTCCAAGCCAGGCTTTACTTCCACCTGGAATCTGGCCAGAGAAGGTGCTTGACATCCTCCAGCACATCCAAACCCTAGACCCGGGGCAGCACGGGGCGGTGGGCTAC
1400      1410      1420      1430      1440      1450      1460      1470      1480      1490      1500      1510      1520
CTGGTGCAGCACACTCTAGAGCACATTGAGCGCAAAAAGGAGGAGGTGGGCGTAGAGGTGAAGCTGCGCTCCGATGAGAAGCACAGAGATGTCTGCTACTCCATCGGGCTCATTATGAAGCATAAGAGGTATGGCTATA
1530      1540      1550      1560      1570      1580      1590      1600      1610      1620      1630      1640      1650      1660
ACTGTGTGATCTACGGCTGGCACCCCACCTGCATGATGGACACGAGTGGATCCGGAACATGAACGTCCACAGCCTGCCCGCACGGCCACCACCAGCCTTTCTATAACGTGCTGGTGGAGGACGGCTCCTGTCGATACGC
1670      1680      1690      1700      1710      1720      1730      1740      1750      1760      1770      1780      1790      1800
AGCCCAAGAAAACTTGGAATATAACGTGGAGCCTCAAGAAATCTCACACCCTGACGTGGGACGCTATTTCTCAGAGTTTACTGGCACTCACTACATCCCAAACGCAGAGCTGGAGATCCGGTATCCAGAAGATCTGGAG
1810      1820      1830      1840      1850      1860      1870      1880      1890      1900      1910      1920      1930      1940
TTTGTCTATGAAACGGTCCAGAATATTTACAGTGCAAAGAAAGAGAACATAGATGAGTAAAGTCTAGAGAGGACATTGCACCTTTGCTGCTGCTGCTATCTTCCAAGAGAACGGGACTCCCGGAAGAAGACGTCTCCACG
1950      1960      1970      1980      1990      2000      2010      2020      2030      2040      2050      2060      2070      2080
GAGCCCTCGGGACCTGCTGCACCAGGAAAGCCACTCCACCAGTAGTGCTGGTTGCCTCCTACTAAGTTTAAATACCGTGTGCTCTTCCCCAGCTGCAAAGACAATGTTGCTCTCCGCCCTACACTAGTGAATTAATCTGA
2090      2100      2110      2120      2130      2140      2150      2160      2170      2180      2190      2200      2210      2220
AAGGCACTGTGTCAGTGGCATGGCTTGTATGCTTGTCCTGTGGTGACAGTTTGTGACATTCTGTCTTCATGAGGTCTCACAGTCGACGCTCCTGTAATCATTCTTTGTATTCACTCCATTCCCCTGTCTGTCTGCATTT
2230      2240      2250      2260      2270      2280      2290      2300      2310      2320      2330      2340      2350      2360
GTCTCAGAACATTTCCTTGGCTGGACAGATGGGGTTATGCATTTGCAATAATTTCCTTCTGATTTCTCTGTGGAACGTGTTCGGTCCCGAGTGAGGACTGTGTGTCTTTTTACCCTGAAGTTAGTTGCATATTCAGAGG
2370      2380      2390      2400      2410      2420      2430      2440      2450      2460      2470      2480      2490      2500
TAAAGTTGTGTGCTATCTTGGCAGCATCTTAGAGATGGAGACATTAACAAGCTAATGGTAATTAGAATCATTTGAATTTATTTTTTTCTAATATGTGAAACACAGATTTCAAGTGTTTTATCTTTTTTTTTTTAAATTTA
2510      2520      2530      2540      2550      2560      2570      2580      2590      2600      2610      2620      2630      2640
AATGGAATATAACACAGTTTTCCCTTCCATATTCCTCTCTTGAGTTTATGCACATCTCTATAAATCATTAGTTTTCTATTTTATTACATAAAATTCTTTTAGAAAATGCAAATAGTGAACTTTGTGAATGGATTTTTC
2650      2660      2670      2680      2690      2700      2710      2720      2730      2740      2750      2760      2770      2780
CATACTCATCTACAATTCCTCCATTTTAAATGACTACTTTTATTTTTTAATTTAAAAAATCTACTTCAGTATCATGAGTAGGTCTTACATCAGTGATGGGTTCTTTTTGTAGTGAGACATACAAATCTGATGTTAATGT
2790      2800      2810      2820      2830      2840      2850      2860      2870      2880      2890      2900      2910
TTGCTCTTAGAAGTCATACTCCATGGTCTTCAAAGACCAAAAAATGAGGTTTTGCCTTTGTAATCAGGAAAAAAAAAAATTAATGAACCTTAAAAAAAAAAAAAAAGGTTTTGAAGGCAAAAAAAGTGGTTTCACACCT
2920      2930      2940      2950      2960      2970      2980      2990      3000      3010      3020      3030      3040      3050
CTTGTTATTCCTTAGAGTCACTTCAAGGCCTGTTTGAATGTGGCAGGTTAGAAAGAGAGAGAATGTCTTTCATTTGAAGAGTGTTGGACTTGTGTGAAAGGCAGATGTGCGTGTTGGAATCTGCTTTTCCAAGCCGCCAG
3060      3070      3080      3090      3100      3110      3120      3130      3140      3150      3160      3170      3180      3190
GGTCCTGACGGCAGCAGGACGAAGCCTGTTGTGGCGTCTTCTGGGAAAGCCTGACCGTGTGTTCGGACGGCACTGGCTCCTTTCCGAAGTTCTCAGTAACTGAGCCCAGAGTAACTGCACGGCTTTGTGCAGCTCTGGA
3200      3210      3220      3230      3240      3250      3260      3270      3280      3290      3300      3310      3320      3330
GCTCCACCAACTCTCGGCCTGCCAGTTCTCAAGCGAGCTAATCTTGTCATTAATCGATAGAAGCTAACTTCCGAAGTTAGGACCTAGTTACTTTGCTCTCAACATTTAAAATAATGCAGTTGCTCTAGTGAATGGGGCG
3340      3350      3360      3370      3380      3390      3400      3410      3420      3430      3440      3450      3460      3470
TTAGGGGCCTGTCTCTGCACCTGTCTGTCCATCTGCATGCAGTATTCTCACCCATGTTGAATGCCTGCTGCTTGTTTACCCTTTGGAAACCCTGGGGTGACCAAGGTTTGGAAAGCCACCTGAGACCACTTCATAGCAA
3480      3490      3500      3510      3520      3530      3540      3550      3560      3570      3580      3590      3600      3610
GGGAAGGCTTTAAGCAGTTACTAGAAAGAGATGGGGATTTGGCCCCTGGCTCCTCCAGCCTGAATGAGCTATTTAATCCACTGTCCATGTTCCTCATCAGTCAAATCCAAAGTCAAAGGATTTGAACCTGCATCTGGAA
3620      3630      3640      3650      3660      3670      3680      3690      3700      3710      3720      3730      3740      3750
ACGTAACCACTCACAGCACCTGGCCCCGCCAAGGTTGGAGGCATTGTACACTACTTTCATTTAAAGGGGAAAGTTTGATAATACGGAATTAATTAATATGAATGAGATGCATTAATAAGAACCTGAGCATGCTGAGAGTT
3760      3770      3780      3790      3800      3810      3820      3830      3840      3850      3860      3870      3880      3890
GCAATTGTTGGTTTTCTGGTTTGATTGATTTCCTTTTTTCTTAGACACATCAAAGTCAAGAAAGATGGTTTTACCTTTACTGACCCAGCTGTACATATGTATCTAGACTGTTTTTAAATGTCTTTCTTCATGAATGCTT
3900      3910      3920      3930      3940      3950      3960      3970      3980      3990      4000      4010      4020      4030
CATGGGGCTCCAGGAAGCCTGTATCACCTGTGTAAGTTGGTATTTGGGCACTTTATATTTTTCTAAAAACGTGTTTTTGGATCCTGTACTCTAATAAATCATAAGTTTCTTTTTAAAAATTTTCCAAAACTTTTCTCCAT
4040      4050      4060      4070      4080      4090      4100      4110      4120      4130      4140      4150      4160
TTTAAAAAGCCCTGTTATAAACGTTGAACTTTCACAATGTTAAAATGTTAAATATTTGGATATAGCAACTTCTTTTCTCTTCAAATGAATGCCAAGATTTTTTTGTACAATGATTAATAAATGGAACTTATCCAGAG
```

FIG. 12B

```
        10        20        30        40        50        60
RSTGFRRAGEEWSR*XLAASPGXLRRPAXTFVLSNLAEVVERVLTFLPAKALLRVACVCR

        70        80        90
LWRECVRRVLRTHRSVTWISAGLAEAGHLXGH
```

FIG. 13A

```
        10        20        30        40        50        60
CCGTAGTACTGGNTTCCGGCGGGCTGGTGAGGAATGGAGCCGGTAGNTGCTTGCGGCGAG

        70        80        90       100       110       120
TCCCGGGNTCCTCCGTAGACCCGCGGANACCTTCGTGTTGAGTAACCTGGCGGAGGTGGT

       130       140       150       160       170       180
GGAGCGTGTGCTCACCTTCCTGCCCGCCAAGGCGTTGCTGCGGGTGGCCTGCGTGTGCCG

       190       200       210       220       230       240
CTTATGGAGGGAGTGTGTGCGCAGAGTATTGCGGACCCATCGGAGCGTAACCTGGATCTC

       250       260       270
CGCAGGCCTGGCGGAGGCCGGCCACCTGGNGGGGCATT
```

FIG. 13B

```
        10        20        30        40        50        60
RPRPVQQQQQQPPQQPPPQPPQQQPPQQQPPPPPQQQQQQQPPPPPPPPPPLPQERNNVG

        70        80        90       100       110       120
ERDDDVPADMVAEESGPGAQNSPYQLRRKTLLPKRTACPTKNSMEGASTSTTENFGHRAK

       130       140       150       160       170       180
RARVSGKSQDLSAAPAEQYLQEKLPDEVVLKIFSYLLEQDLCRAACVCKRFSELANDPNL

       190
WKRLYMEVFEYTRPMMH
```

FIG. 14A

```
        10        20        30        40        50        60
GCGGCCGCGCCCGGTGCAGCAACAGCAGCAGCAGCCCCCGCAGCAGCCGCCGCCGCAGCC

        70        80        90       100       110       120
GCCCCAGCAGCAGCCGCCCCAGCAGCAGCCTCCGCCGCCGCCGCAGCAGCAGCAGCAGCA

       130       140       150       160       170       180
GCAGCCTCCGCCGCCGCCACCGCCGCCTCCGCCGCTGCCTCAGGAGCGGAACAACGTCGG

       190       200       210       220       230       240
CGAGCGGGATGATGATGTGCCTGCAGATATGGTTGCAGAAGAATCAGGTCCTGGTGCACA

       250       260       270       280       290       300
AAATAGTCCATACCAACTTCGTAGAAAAACTCTTTTGCCGAAAAGAACAGCGTGTCCCAC

       310       320       330       340       350       360
AAAGAACAGTATGGAGGGCGCCTCAACTTCAACTACAGAAAACTTTGGTCATCGTGCAAA

       370       380       390       400       410       420
ACGTGCAAGAGTGTCTGGAAAATCACAAGATCTATCAGCAGCACCTGCTGAACAGTATCT

       430       440       450       460       470       480
TCAGGAGAAACTGCCAGATGAAGTGGTTCTAAAAATCTTCTCTTACTTGCTGGAACAGGA

       490       500       510       520       530       540
TCTTTGTAGAGCAGCTTGTGTATGTAAACGCTTCAGTGAACTTGCTAATGATCCCAATTT

       550       560       570       580       590
GTGGAAACGATTATATATGGAAGTATTTGAATATACTCGCCCTATGATGCAT
```

FIG. 14B

```
          10        20        30        40        50        60
RPRPGLRGGRAPCEVTMEAGGLPLELWRMILAYLHLPDLGRCSLVCRAWYELILSLDSTR

          70        80        90       100       110       120
WRQLCLGCTECRHPNWPNQPDVEPESWREAFKQHYLASKTWTKNALDLESSICFSLFRRR

         130       140       150       160       170
RERRTLSVGPGREFDSLGSALAMASLYDRIVLFPGVYEEQGEIILKVPVEIVGQGKLG
```

FIG. 15A

```
         10         20         30         40         50         60
GCGGCCGCGGCCCGGACTCCGCGGTGGGCGAGCGCCCTGTGAGGTGACCATGGAGGCTGG

         70         80         90        100        110        120
TGGCCTCCCCTTGGAGCTGTGGCGCATGATCTTAGCCTACTTGCACCTTCCCGACCTGGG

        130        140        150        160        170        180
CCGCTGCAGCCTGGTATGCAGGGCCTGGTATGAACTGATCCTCAGTCTCGACAGCACCCG

        190        200        210        220        230        240
CTGGCGGCAGCTGTGTCTGGGTTGCACCGAGTGCCGCCATCCCAATTGGCCCAACCAGCC

        250        260        270        280        290        300
AGATGTGGAGCCTGAGTCTTGGAGAGAAGCCTTCAAGCAGCATTACCTTGCATCCAAGAC

        310        320        330        340        350        360
ATGGACCAAGAATGCCTTGGACTTGGAGTCTTCCATCTGCTTTTCTCTATTCCGCCGGAG

        370        380        390        400        410        420
GAGGGAACGACGTACCCTGAGTGTTGGGCCAGGCCGTGAGTTTGACAGCCTGGGCAGTGC

        430        440        450        460        470        480
CTTGGCCATGGCCAGCCTGTATGACCGAATTGTGCTCTTCCCAGGTGTGTACGAAGAGCA

        490        500        510        520        530
AGGTGAAATCATCTTGAAGGTGCCTGTGGAGATTGTAGGGCAGGGGAAGTTGGGTGA
```

FIG. 15B

```
              10        20        30        40        50        60
ETETAPLTLESLPTDPLLLILSFLDYRDLINCCYVSRRLSQLSSHDPLWRRHCKKYWLIS

              70        80        90       100       110       120
EEEKTQKNQCWKSLFIDTYSDVGRYIDHYAAIKKASGMISRNIWSPGVLGWVLSLKEGCS

             130       140       150       160       170       180
RGRPRCCGSADWAASFLDDYRCSYRIHNGQKLVGSWGYWEAWHCLITIVLKIC*TSIQLP

             190       200       210       220       230       240
EIPAETGTEILSPFNFCIHTGLSQYIAVEAAEG*NKNEVFYQCQTVERVFKYGIKMCSDG

             250
CINGMH*VFS
```

FIG. 16A

```
        10         20         30         40         50         60
GAGACCGAGACGGCGCCGCTGACCCTAGAGTCGCTGCCCACCGATCCCCTGCTCCTCATC

        70         80         90        100        110        120
TTATCCTTTTTGGACTATCGGGATCTAATCAACTGTTGTTATGTCAGTCGAAGATTAAGC

       130        140        150        160        170        180
CAGCTATCAAGTCATGATCCGCTGTGGAGAAGACATTGCAAAAAATACTGGCTGATATCT

       190        200        210        220        230        240
GAGGAAGAGAAAACACAGAAGAATCAGTGTTGGAAATCTCTCTTCATAGATACTTACTCT

       250        260        270        280        290        300
GATGTAGGAAGATACATTGACCATTATGCTGCTATTAAAAAGGCCTCGGGAATGATCTCA

       310        320        330        340        350        360
AGAAATATTTGGAGCCCAGGTGTCCTCGGATGGGTTTTATCTCTGAAAGAGGGGTGCTCG

       370        380        390        400        410        420
AGAGGAAGACCTCGATGCTGTGGAAGCGCAGATTGGGCTGCAAGTTTCCTGGACGATTAT

       430        440        450        460        470        480
CGATGTTCATACCGAATTCACAATGGACAGAAGTTAGTTGGTTCCTGGGGTTATTGGGAA

       490        500        510        520        530        540
GCATGGCACTGTCTAATCACTATCGTTCTGAAGATTTGTTAGACGTCGATACAGCTGCCG

       550        560        570        580        590        600
GAGATTCCAGCAGAGACAGGGACTGAAATACTGTCTCCCTTTAACTTTTGCATACATACT

       610        620        630        640        650        660
GGTTTGAGTCAGTACATAGCAGTGGAAGCTGCAGAGGGTTGAAACAAAAATGAAGTTTTC

       670        680        690        700        710        720
TACCAATGTCAGACAGTAGAACGTGTGTTTAAATATGGCATTAAGATGTGTTCTGATGGT

       730        740        750
TGTATAAATGGCATGCATTAGGTATTTTCAG
```

FIG. 16B

```
             10         20         30         40         50         60
GSGFRAGGWPLTMPGKHQHFQEPEVGCCGKYFLFGFNIVFWVLGALFLAIGLWAWGEKGV

             70         80         90        100        110        120
LSNISALTDLGGLDPVWLVCGSWRRHVGAGLCWAAIGALRENTFLLKFFXXFLGLIFFLE

LA
```

FIG. 17A

```
         10        20        30        40        50        60
GGCTCCGGTTTCCGGGCCGGCGGGTGGCCGCTCACCATGCCCGGNAAGCACCAGCATTTC

         70        80        90       100       110       120
CAGGAACCTGAGGTCGGCTGCTGCGGAAATACTTCCTGTTTGGCTTCAACATTGTCTTC

        130       140       150       160       170       180
TGGGTGCTGGGAGCCCTGTTCCTGGCTATCGGCCTCTGGGCCTGGGGTGAGAAGGGCGTT

        190       200       210       220       230       240
CTCTCGAACATCTCAGCGCTGACAGATCTGGGAGGCCTTGACCCCGTGTGGCTTGTTTGT

        250       260       270       280       290       300
GGTAGTTGGAGGCGTCATGTCGGTGCTGGGCTTTGCTGGGCTGCAATTGGGGCCCTCCGG

        310       320       330       340       350       360
GAGAACACCTTCCTGCTCAAGTTTTTCTNCGNGTTCCTCGGTCTCATCTTCTTCCTGGAG

CTGGCAAC
```

FIG. 17B

```
         10        20        30        40        50        60
AAAAAAYLDELPEPLLLRVLAALPAAELVQACRLVCLRWKELVDGAPLWLLKCQQEGLVP

         70        80        90       100       110       120
EGGVEEERDHWQQFYFLSKRRRNLLRNPCGEEDLEGWCDVEHGGDGWRVEELPGDSGVEF

        130       140       150       160       170       180
THDESVKKYFASSFEWCRKAQVIDLQAEGYWEELLDTTQPAIVVKDWYSGRSDAGCLYEL

        190       200       210       220       230       240
TVKLLSEHENVLAEFSSGQVAVPQDSDGGGWMEISHTFTDYGPGVRFVRFEHGGQGSVYW

        250
KGWFGARVTNSSVWVEP*
```

FIG. 18A

```
           10        20        30        40        50        60
   GCGGCGGCCGCCGCCGCGTACCTGGACGAGCTGCCCGAGCCGCTGCTGCTGCGCGTGCTGGCCGCACTG

  70        80        90       100       110       120       130
   CCGGCCGCCGAGCTGGTGCAGGCCTGCCGCCTGGTGTGCCTGCGCTGGAAGGAGCTGGTGGACGGCGCC

  140       150       160       170       180       190       200
   CCGCTGTGGCTGCTCAAGTGCCAGCAGGAGGGGCTGGTGCCCGAGGGCGGCGTGGAGGAGGAGCGCGAC

   210       220       230       240       250       260       270
   CACTGGCAGCAGTTCTACTTCCTGAGCAAGCGGCGCCGCAACCTTCTGCGTAACCCGTGTGGGGAAGAG

    280       290       300       310       320       330       340
   GACTTGGAAGGCTGGTGTGACGTGGAGCATGGTGGGGACGGCTGGAGGGTGGAGGAGCTGCCTGGAGAC

     350       360       370       380       390       400       410
   AGTGGGGTGGAGTTCACCCACGATGAGAGCGTCAAGAAGTACTTCGCCTCCTCCTTTGAGTGGTGTCGC

      420       430       440       450       460       470       480
   AAAGCACAGGTCATTGACCTGCAGGCTGAGGGCTACTGGGAGGAGCTGCTGGACACGACTCAGCCGGCC

       490       500       510       520       530       540       550
   ATCGTGGTGAAGGACTGGTACTCGGGCCGCAGCGACGCTGGTTGCCTCTACGAGCTCACCGTTAAGCTA

        560       570       580       590       600       610       620
   CTGTCCGAGCACGAGAACGTGCTGGCTGAGTTCAGCAGCGGGCAGGTGGCAGTGCCCCAAGACAGTGAC

         630       640       650       660       670       680       690
   GGCGGGGGCTGGATGGAGATCTCCCACACCTTCACCGACTACGGGCCGGGCGTCCGCTTCGTCCGCTTC

          700       710       720       730       740       750
   GAGCACGGGGGGCAGGGCTCCGTCTACTGGAAGGGCTGGTTCGGGGCCCGGGTGACCAACAGCAGCGTG

 760       770
   TGGGTAGAACCCTGA
```

FIG. 18B

```
       10        20        30        40        50        60
MGEKAVPLLRRRRVKRSCPSCGSELGVEEKRGKGNPISIQLFPPELVEHIISFLPVRDLV

       70        80        90       100       110       120
ALGQTCRYFHEVCDGEGVWRRICRRLSPRLQDQDTKGLYFQAFGGRRRCLSKSVAPLLAH

      130       140       150       160       170       180
GYRRFLPTKDHVFILDYVGTLFFLKNALVSTLGQMQWKRACRYVVLCRGAKDFASDPRCD

      190       200       210       220       230       240
TVYRKYLYVLATREPQEVVGTTSSRACDCVEVYLQSSGQRVFKMTFHHSMTFKQIVLVGQ

      250       260       270       280       290       300
ETQRALLLLTEEGKIYSLVVNETQLDQPRSYTVQLALRKVSHYLPHLRVACMTSNQSSTL

      310
YVTDPILCSWLQPPWPGG
```

FIG. 19A

```
         10        20        30        40        50        60
ATGGGCGAGAAGGCGGTCCCTTTGCTAAGGAGGAGGCGGGTGAAGAGAAGCTGCCCTTCTTGTGGCTCG

70        80        90       100       110       120       130
GAGCTTGGGGTTGAAGAGAAGAGGGGGAAAGGAAATCCGATTTCCATCCAGTTGTTCCCCCCAGAGCTG

140       150       160       170       180       190       200
GTGGAGCATATCATCTCATTCCTCCCAGTCAGAGACCTTGTTGCCCTCGGCCAGACCTGCCGCTACTTC

210       220       230       240       250       260       270
CACGAAGTGTGCGATGGGGAAGGCGTGTGGAGACGCATCTGTCGCAGACTCAGTCCGCGCCTCCAAGAT

 280       290       300       310       320       330       340
CAGGACACGAAGGGCCTGTATTTCCAGGCATTTGGAGGCCGCCGCCGATGTCTCAGCAAGAGCGTGGCC

  350       360       370       380       390       400       410
CCCTTGCTAGCCCACGGCTACCGCCGCTTCTTGCCCACCAAGGATCACGTCTTCATTCTTGACTACGTG

   420       430       440       450       460       470       480
GGGACCCTCTTCTTCCTCAAAAATGCCCTGGTCTCCACCCTCGGCCAGATGCAGTGGAAGCGGGCCTGT

    490       500       510       520       530       540       550
CGCTATGTTGTGTTGTGTCGTGGAGCCAAGGATTTTGCCTCGGACCCAAGGTGTGACACAGTTTACCGT

     560       570       580       590       600       610       620
AAATACCTCTACGTCTTGGCCACTCGGGAGCCGCAGGAAGTGGTGGGTACCACCAGCAGCCGGGCCTGT

      630       640       650       660       670       680       690
GACTGTGTTGAGGTCTATCTGCAGTCTAGTGGGCAGCGGGTCTTCAAGATGACATTCCACCACTCAATG

       700       710       720       730       740       750
ACCTTCAAGCAGATCGTGCTGGTTGGTCAGGAGACCCAGCGGGCTCTACTGCTCCTCACAGAGGAAGGA

760       770       780       790       800       810       820
AAGATCTACTCTTTGGTAGTGAATGAGACCCAGCTTGACCAGCCACGCTCCTACACGGTTCAGCTGGCC

830       840       850       860       870       880       890
CTGAGGAAGGTGTCCCACTACCTGCCTCACCTGCGCGTGGCCTGCATGACTTCCAACCAGAGCAGCACC

900       910       920       930       940       950
CTCTACGTCACAGATCCTATTCTGTGCTCTTGGCTACAACCACCTTGGCCTGGTGGATGA
```

FIG. 19B

```
         10        20        30        40        50        60
RGGSEGRGRGREKRARGARRKRKQGGREARAADGEGGSGPGAEAGARTRPREEAEGGGSV

         70        80        90       100       110       120
EEGARGIIKGDEGSVGAGKEAQGRKYGKEEWRVRARRREGARPGRVQGQGGQVWAYIPGT

        130       140       150       160       170       180
GAAMAAAAREEEEEAARESAACPAAGPALWRLPEVLLLHMCSYLDMRALGRLAQVYRWLW

        190       200       210       220       230       240
HFTNCDLLRRQIAWASLNSGFTRLGTNLMTSVPVKVSQNWIVGCCREGILLKWRCSQMPW

        250       260       270       280       290       300
MQLEDDALYISQANFILAYQFRPDGASLNRQPLGVSAGHDEDVCHFVLATSHIVSAGGDG

        310       320       330       340       350       360
KIGLGKIHSTFAAKYWAHEQEVNCVDCKGGIISFGSRDRTAKVWPLASGQLGQCLYTIQT

        370       380       390       400       410       420
EDQIWSVAIRPLLSSFVTGTACCGHFSPLKIWDLNSGQLMTHLDRDFPPRAGVLDVIYES

        430       440       450       460       470       480
PFALLSCGYDTYVRYWDCRTSVRKCVMEWEEPHNSTLYCLQTDGNHLLATGSSFYSVVRL

        490       500       510       520       530
WDRHQRACPHTFPLTSTRLGSPVYCLHLTTKHLYAALSYNLHVLDIQNP*
```

FIG. 20A

```
        10        20        30        40        50        60        70        80        90
CGAGGGGGAAGCGAAGGAAGGGGAAGAGGAAGGGAAAAGCGAGCGAGAGGGGCAAGGCGGAAGAGGAAGCAGGGCGGAAGGGAAGCCCGGGCCG

   100       110       120       130       140       150       160       170       180
CAGACGGCGAAGGAGGCAGCGGGCCGGGGGCTGAGGCGGGAGCGAGGACACGCCCAAGAGAGGAAGCAGAGGGAGGCGGAAGCGTGGAGGAAGG

190      200       210       220       230       240       250       260       270       280
GGCGAGAGGCATCATCAAAGGAGATGAGGGGAGCGTAGGGGCCGGGAAAGAGGCACAAGGAAGAAAGTATGGGAAGGAGGAATGGAGGGTCAGG

     290       300       310       320       330       340       350       360       370
GCTAGGCGGCGGGAGGGCGCCAGGCCGGGAAGAGTACAAGGACAAGGAGGTCAGGTTTGGGCCTACATCCCGGGGACAGGGGCGGCCATGGCGG

 380       390       400       410       420       430       440       450       460       470
CGGCAGCCAGGGAGGAGGAGGAGGAGGCGGCTCGGGAGTCAGCCGCCTGCCCGGCTGCGGGGCCAGCGCTCTGGCGCCTGCCGGAAGTGCTGCT

       480       490       500       510       520       530       540       550       560
GCTGCACATGTGCTCCTACCTCGACATGCGGGCCCTCGGCCGCCTGGCCCAGGTGTACCGCTGGCTGTGGCACTTCACCAACTGCGACCTGCTC

   570       580       590       600       610       620       630       640       650
CGGCGCCAGATAGCCTGGGCCTCGCTCAACTCCGGCTTCACGCGGCTCGGCACCAACCTGATGACCAGTGTCCCAGTGAAGGTGTCTCAGAACT

660      670       680       690       700       710       720       730       740       750
GGATAGTGGGGTGCTGCCGAGAGGGGATTCTGCTGAAGTGGAGATGCAGTCAGATGCCCTGGATGCAGCTAGAGGATGATGCTTTGTACATATC

     760       770       780       790       800       810       820       830       840
CCAGGCTAATTTCATCCTGGCCTACCAGTTCCGTCCAGATGGTGCCAGCTTGAACCGTCAGCCTCTGGGAGTCTCTGCTGGGCATGATGAGGAC

 850       860       870       880       890       900       910       920       930       940
GTTTGCCACTTTGTGCTGGCCACCTCGCATATTGTCAGTGCAGGAGGAGATGGGAAGATTGGCCTTGGTAAGATTCACAGCACCTTCGCTGCCA

       950       960       970       980       990      1000      1010      1020      1030
AGTACTGGGCTCATGAACAGGAGGTGAACTGTGTGGATTGCAAAGGGGGCATCATATCATTTGGCTCCAGGGACAGGACGGCCAAGGTGTGGCC

  1040      1050      1060      1070      1080      1090      1100      1110      1120
TTTGGCCTCAGGCCAGCTGGGGCAGTGTTTATACACCATCCAGACTGAAGACCAAATCTGGTCTGTTGCTATCAGGCCATTACTCAGCTCTTTT

1130    1140      1150      1160      1170      1180      1190      1200      1210      1220
GTGACAGGGACGGCTTGTTGTGGGCACTTCTCACCCCTGAAAATCTGGGACCTCAACAGTGGGCAGCTGATGACACACTTGGACAGAGACTTTC

    1230      1240      1250      1260      1270      1280      1290      1300      1310
CCCCAAGGGCTGGGGTGCTGGATGTCATATATGAGTCCCCTTTCGCACTGCTCTCCTGTGGCTATGACACCTATGTTCGCTACTGGGACTGCCG

1320      1330      1340      1350      1360      1370      1380      1390      1400      1410
CACCAGTGTCCGGAAATGTGTCATGGAGTGGGAGGAGCCCCACAACAGCACCCTGTACTGCCTGCAGACAGATGGCAACCACTTGCTTGCCACA

      1420      1430      1440      1450      1460      1470      1480      1490      1500
GGTTCCTCCTTCTATAGCGTTGTACGGCTGTGGGACCGGCACCAAAGGGCCTGCCCGCACACCTTCCCGCTGACGTCGACCCGCCTCGGCAGCC

  1510      1520      1530      1540      1550      1560      1570      1580      1590
CTGTGTACTGCCTGCATCTCACCACCAAGCATCTCTATGCTGCGCTGTCTTACAACCTCCACGTCCTGGATATTCAAAACCCGTGA
```

FIG. 20B

```
         10        20        30        40        50        60
LILTSVLLFQRHGYCTLGEAFNRLDFSSAIQDIRTFNYVVKLLQLIAKSQLTSLSGVAQK

         70        80        90       100       110       120
NYFNILDKIVQKVLDDHHNPRLIKDLLQDLSSTLCILIRGVGKSVLVGNINIWICRLETI

        130       140       150       160       170       180
LAWQQQLQDLQMTKQVNNGLTLSDLPLHMLNNILYRFSDGWDIITLGQVTPTLYMLSEDR

        190       200       210       220       230       240
QLWKKLCQYHFAEKQFCRHLILSEKGHIEWKLMYFALQKHYPAKEQYGDTLHFCRHCSIL

        250       260       270
FWKDSGHPCTAADPDSCFTPVSPQHFIDLFKF
```

FIG. 21A

```
          10        20        30        40        50        60
GCATTGCTATAATTTTACTATACTCTCATCTAAATCTAAAATCAGTCTTCAAAATAAAAACAAATTGTC

70        80        90        100       110       120       130
CTTTGCCAAAAATTTTTTTAATCGCACAATTAATTGACATTAACTGCCAATTCTTTTTGGCTAATTGAC

140       150       160       170       180       190       200
TAATTTTAACTTCTGTGTTGCTTTTCCAGAGGCATGGCTATTGCACCTTGGGAGAAGCCTTTAATCGGT

210       220       230       240       250       260       270
TAGACTTCTCAAGTGCAATTCAAGATATCCGAACGTTCAATTATGTGGTCAAACTGTTGCAGCTAATTG

280       290       300       310       320       330       340
CAAAATCCCAGTTAACTTCATTGAGTGGCGTGGCACAGAAGAATTACTTCAACATTTTGGATAAAATCG

350       360       370       380       390       400       410
TTCAAAAGGTTCTTGATGACCACCACAATCCTCGCTTAATCAAAGATCTTCTGCAAGACCTAAGCTCTA

420       430       440       450       460       470       480
CCCTCTGCATTCTTATTAGAGGAGTAGGGAAGTCTGTATTAGTGGGAAACATCAATATTTGGATTTGCC

490       500       510       520       530       540       550
GATTAGAAACTATTCTCGCCTGGCAACAACAGCTACAGGATCTTCAGATGACTAAGCAAGTGAACAATG

560       570       580       590       600       610       620
GCCTCACCCTCAGTGACCTTCCTCTGCACATGCTGAACAACATCCTATACCGGTTCTCAGACGGATGGG

630       640       650       660       670       680       690
ACATCATCACCTTAGGCCAGGTGACCCCCACGTTGTATATGCTTAGTGAAGACAGACAGCTGTGGAAGA

700       710       720       730       740       750
AGCTTTGTCAGTACCATTTTGCTGAAAAGCAGTTTTGTAGACATTTGATCCTTTCAGAAAAAGGTCATA

760       770       780       790       800       810       820
TTGAATGGAAGTTGATGTACTTTGCACTTCAGAAACATTACCCAGCGAAGGAGCAGTACGGAGACACAC

830       840       850       860       870       880       890
TGCATTTCTGTCGGCACTGCAGCATTCTCTTTTGGAAGGACTCAGGACACCCCTGCACGGCGGCCGACC

900       910       920       930       940       950       960
CTGACAGCTGCTTCACGCCTGTGTCTCCGCAGCACTTCATCGACCTCTTCAAGTTTTAAGGGCTGCCCC

970       980       990       1000      1010      1020      1030
TGCCATCCCTATTGGAGATTGTGAATCCTGCTGTCTGTGCAGGGCTCATAGTGAGTGTTCTGTGAGGTG

1040      1050      1060      1070      1080      1090      1100
GGTGGAGACTCCTCGGAAGCCCCTGCTTCCAGAAAGCCTGGGAAGAACTGCCCTTCTGCAAAGGGGGA

1110      1120      1130      1140      1150      1160      1170
CTGCATGGTTGCATTTTCATCACTGAAAGTCAGAGGCCAAGGAAATCATTTCTACTTCTTTAAAAACTC

1180      1190      1200      1210
CTTCTAAGCATATTAAAATGTGAAATTTTGCGTACTCTCTC
```

FIG. 21B

```
          10        20        30        40        50        60
YGSEGKGSSSISSDVSSSTDHTPTKAQKNVATSEDSDLSMRTLSTPSPALICPPNLPGFQ

          70        80        90       100       110       120
NGRGSSTSSSSITGETVAMVHSPPPTRLTHPLIRLASRPQKEQASIDRLPDHSMVQIFSF

         130       140       150       160       170       180
LPTNQLCRCARVCRRWYNLAWDPRLWRTIRLTGETINVDRALKVLTRRLCQDTPNVCLML

         190       200       210       220       230       240
ETVTVSGCRRLTDRGLYTIAQCCPELRRLEVSGCYNISNEAVFDVVSLCPNLEHLDVSGC

         250       260       270       280       290       300
SKVTCISLTREASIKLSPLHGKQISIRYLDMTDCFVLEDEGLHTIAAHCTQLTHLYLRRC

         310       320       330       340       350       360
VRLTDEGLRYLVIYCASIKELSVSDCRFVSDFGLREIAKLESRLRYLSIAHCGRVTDVGI

         370       380       390       400       410       420
RYVAKYCSKLRYLNARGCEGITDHGVEYLAKNCTKLKSLDIGKCPLVSDTGLECLALNCF

         430       440       450       460       470       480
NLKRLSLKSCESITGQGLQIVAANCFDLQTLNVQDCEVSVEALRFVKRHCKRCVIEHTNP

AFF
```

FIG. 22A

10 20 30 40 50 60 70 80 90 100 110 120 130
AGTACGGCAGTGAGGGCAAAGGCAGCTCGAGCATCTCATCTGACGTGAGTTCAAGTACAGATCACACGCCCACTAAAGCCCAGAAGAATGTGGCTACCAGCGAAGACTCCGACCTGAGCATGCCCACACTGAGCACGCC

140 150 160 170 180 190 200 210 220 230 240 250 260 270
CAGCCCAGCCCTGATATGTCCACCGAATCTCCCAGGATTTCAGAATGGAAGGGGCTGGTCCACCTCCTCGTCCTCCATCACCGGGGAGACGGTGGCCATGGTGCACTCCCCGCCCCCGACCCCGCTCACACACCCCGCTC

280 290 300 310 320 330 340 350 360 370 380 390 400 410
ATCCGGCTCCCCTCCAGACCCCAGAAGGAGCAGGCCAGCATAGACCGGCTCCCGGACCACTCCATGGTGCAGATCTTCTCCTTCCTGCCCACCAACCAGCTGTGCCGCTGCGCGGAGTGTGCCGCCCCTGGTACAACC

420 430 440 450 460 470 480 490 500 510 520 530 540 550
TGGCCTGGGACCCGCGGCTCTGGAGCACTATCCGCCTGACGGGCGAGACCATCAACGTGGACCGCGCCCTCAAGGTGCTGACCCGCAGACTCTGCCAGGACACCCCCAACGTGTGTCTCATGCTGGAAACCGTAACTGT

560 570 580 590 600 610 620 630 640 650 660 670 680 690
CAGTGGCTGCAGGCGGCTCACAGACCGAGGGCTGTACACCATCGCCCAGTGCTGCCCCGAACTGAGGCGACTGGAAGTCTCAGGCTGTTACAATATCTCCAACGAGGCCGTCTTTGATGTGGTGTCCCTCTGCCCTAAT

700 710 720 730 740 750 760 770 780 790 800 810 820 830
CTGGAGCACCTGGATGTGTCAGGATGCTCCAAAGTGACCTGCATCAGCTTGACCCGGGAGGCCTCCATTAAACTGTCACCCTTGCATGGCAAACAGATTTCCATCCCGCTACCTGGACATGACCGACTGCTTCGTGCTGG

840 850 860 870 880 890 900 910 920 930 940 950 960 970
AGGACGAAGGCCTGCACACCATCGCGGGGCACTGCACGCAGCTCACCCACCTCTACCTGCGCCGCTGCGTCCGCCTGACCGACGAAGGCCTGCGCTACCTGGTGATCTACTGCCCCTCCATCAAGGAGCTGAGCGTCAG

980 990 1000 1010 1020 1030 1040 1050 1060 1070 1080 1090 1100 1110
CGACTGCCGCTTCGTCAGCGACTTCGGCCTGCGGGAGATCGCCAAGCTGGAGTCCCGCCTGCGGTACCTGAGCATCGCGCACTGCGGCCGGGTCACCGACGTGGGCATCCGCTACGTGGCCAAGTACTGCAGCAAGCTG

1120 1130 1140 1150 1160 1170 1180 1190 1200 1210 1220 1230 1240 1250
CGCTACCTCAACGCGAGGGGCTGCGAGGGCATCACGGACCACGGTGTGGAGTACCTGGCCAAGAACTGCACCAAACTCAAATCCCTGGATATCGGCAAATGCCCTTTGGTATCCGACACGGGCCTGGAGTGCCTGGCCC

1260 1270 1280 1290 1300 1310 1320 1330 1340 1350 1360 1370 1380 1390
TGAACTGCTTCAACCTCAAGCGGCTCAGCCTCAAGTCCTGCGAGAGCATCACCGGCCAGGGCTTGCAGATCGTGGCCGCCAACTGCTTTGACCTCCAGACGCTGAATGTCCAGGACTGCGAGGTCTCCGTGGAGGCCCT

1400 1410 1420 1430 1440 1450 1460 1470 1480 1490 1500 1510 1520
GCGCTTTGTCAAACGCCCACTGCAAGCGCTGCGTCATCGAGCACACCAACCCGGCTTTCTTCTGAAGGGACAGAGTTCATCCGGCGTTGTATTCACACAAACCTGAACAAAGCAAATTTTTTTAAAAGCAGCGTATGTAA

1530 1540 1550 1560 1570 1580 1590 1600 1610 1620 1630 1640 1650 1660
GCACCGACACCCACTCAAAACAGCTCTTTCTTCCGGGAAGGTTATTAGGAATCTGGCCTTTATTTTTCCTCATTTCTCATGGCAACAGAGGCCAAAGAAACGAAGCAAGACAAACAGCAAACAGGCATTTTGGTCAGG

1670 1680 1690 1700 1710 1720 1730 1740 1750 1760 1770 1780 1790 1800
TCATTTGTAGGCAGTTTCTCTTCTCACAAAAGATGTACTTAAGCAGGCTGATCGCTGTTCCTTGAGCAAGGCGCTTACTCTCCTCCCGCTCAGGCCCCCAAGGCCGCCCTTTCCCTCCGCACACAGGCCCCACCCCCACAG

1810 1820 1830 1840 1850 1860 1870 1880 1890 1900 1910 1920 1930 1940
TTCCACCCCCCCCCCCCAAGGCCACACCCTCCCTCCCTAGAGCAGCAGCGAGGATCCATCATCAGAATCACAGTGCTCTCCAGACCTCCTCTCTAAACTGCTTCATTGACCTAAGTCACTCTCTTCAATCCCACACCCA

1950 1960 1970 1980 1990 2000 2010 2020 2030 2040 2050 2060 2070 2080
TGGACATTCTTGTCAACTCAATACCATAGCACTTTGCATAGGCAAAATACTTTTCAGGCCTTTTTAAAAAATTCATTACAGCAAACAGCTGGGGAAGGACATGCAGTCCTCCCCCAGCTCTGTCAATGACTATGACCTT

2090 2100 2110 2120 2130 2140 2150 2160 2170 2180 2190 2200 2210 2220
GGCCAAAGCACTTCACTGCTCTGGGCTGCAGCTTCCAGCACTGAATCAGAGGCCACACAGCCCAAAGATTAGCTTCATGTCCATTATAGCATTGAGGGAGCAGAGATACCCATACACAGAAGCACCTTGGCATAGAGCA

2230 2240 2250 2260 2270 2280 2290 2300 2310 2320 2330 2340 2350 2360
CCCAGGCATCGACCTCTTCCAGGAGAACTGATTCTGTGGATGGATGTGATTTCAGGAGATTGTGCAGTGCCAGCATCAGTGCATAAAGGGTCCTGTATGTCCTTTGGCTGCAAATCACCCACTTCCCTGTGTTTCAGTG

2370 2380 2390 2400 2410 2420 2430 2440 2450 2460 2470 2480 2490 2500
GGAGAATTTCCTCTCCCACCTCCTCACATCCTCTTTTGCCAGGCTGGATGCTGTCGTCTCTGTACACAAATACTTTCTGCATTCCCCCCTCCACACCATCCTAGCGAGGCACCAGCACACCTAATCACAGCAAAGCCCA

2510 2520 2530 2540 2550 2560 2570 2580 2590 2600 2610 2620 2630 2640
CATCCCCCCCATCAGTTGCTTTTACTCAGTGTTTTCAAATAGGAGTAAAGCCCCTTGCAATTTTTAATTAACAAGCAAGGCCCAAGGGAACACATGTCCTCAAAAGTTTTTCTGATCCCTCGCCTTGCACACCTGGCATG

2650 2660 2670 2680 2690 2700 2710 2720 2730 2740 2750 2760 2770 2780
CATCAGGCACATCTGTCCTACAGCTGGCAGAGACAGATGCCTCGGTTCTTTGTCATTCAGATTGCATTTGACCTCTTCTCATCTATTTATTTCTTTATACATCCAGACTTCATCACATGAAGCCTATTGGGGTTAAGTT

2790 2800 2810 2820 2830 2840 2850 2860 2870 2880 2890 2900 2910
TGTAAGTGTTTAATTGTGCAAATTGCCACCCTGTGTACCTCCTCCATGTCTGTCTGCGTGTTTTCCACCAAAGAATGCAAAGCAGACTTCCAGGTGTTTAAATTCTGTTCACTCAACAATGCCAGATGAATGGAAGAGG

2920 2930 2940 2950 2960 2970 2980 2990 3000 3010 3020 3030 3040 3050
CAACACACTGAGATGACTTAGACTCTGGTCCACCAACCAGACCCTTGGAAAGGAATACTAAAATCATTACAAGGTATGGATTTTAAATGGATGAAACTTCAAATTATCTTATTTGGATAGAAGTCTATATTCTAGCCTC

3060 3070 3080 3090 3100 3110 3120 3130 3140 3150 3160 3170 3180 3190
ATTTGCATGAAGTCAGATAGCCAGAAGAAATTCCATTGCTGGTTTTCACGAAATTCACTTGTCTTTTGCTAATAAACACATGGCCCTTTCCCAGATTATTCTCTAGCCAAGCCCCACCTTTGTTACGTTGAAATCCCTC

3200 3210 3220 3230 3240 3250 3260 3270 3280 3290 3300 3310 3320 3330
ATTTATTTTCTTCTCAAAATGCCCATTATCCAAATGCAGAACCTCTGCATCTCCAAGCCAGTTATGCTGAATTTGTCAAACTTAGACACCCTTGACAACTGCACTCCTACTGTAGGCTCCTGTGCATACTGTCGTCTTC

3340 3350 3360 3370 3380 3390 3400 3410 3420 3430 3440 3450 3460 3470
TGTGGGGATGGAGAGGTTAGTGTGATGAGGTGGTGTCTGCCCAGGAGGTTTCTTTCAAACATCATGGCCTCCCATCCAATCAACATCATCAAATTACATGTGTAATCAAGGCTCTGTGCCATGGGGAAATGAATCAT

3480 3490 3500 3510 3520 3530 3540 3550 3560 3570 3580 3590 3600 3610
TTAGCTAGGCCAGGATCTAGTGAAAGCCACAGAGTTTAAAACCATGAAAGAAGTTGAAGGCAGCATTCCTCAGCTCTGTGACTTGTGACCCTATTTGAAGTTTCAGGATTTGGGTGTCACAAAGGATTGTCCCTAATCC

3620 3630 3640 3650 3660 3670 3680 3690 3700 3710 3720 3730 3740 3750
TTGGCCCTGGGGTCTTCCGAGTGAGCTGGTTTAATACTCTGAGAATGAGCAGGGAGATCCAGAGAATGAATCCCTGACCGCATCACCTAAACTGTCTTCCAAACATGAGACAAAGCTGACTGTTCACACTGATTGCCCA

3760 3770 3780 3790 3800 3810 3820 3830 3840 3850 3860 3870 3880 3890
GCACATACCGTCTTGCCAGTTTCTTCTTTTCTCCCAGTCTCCTGTTCATCCATTCTGTTCTCCCTTGGGTGGAATCTATGATGGAGGTTACTGGGGAAACAGCTCAGCAGATTTTTGGAGACCAAACCAAAGGTCTC

3900 3910 3920 3930 3940 3950 3960 3970 3980 3990 4000 4010 4020 4030
ACTAGGAAATTTATCTGTTTTAAAACATTGCTTCCTTCCTGGCTCTGCTAAATTGAATGCTCATTGTTTGTTGTTGTTGTTTTTTTAATTCTAATGTTCAAATCACTGCGTGCTGTATGAATCTAGAAAGCCTTAATTTA

4040 4050
CTACCAAGAAATAAAGCAATATGTTCGT

FIG. 22B

```
         10         20         30         40         50         60
AAAPAPAPAPTPTPEEGPDAGWGDRIPLEILVQIFGLLVAADGPMPFLGRAARVCRRWQE

         70         80         90        100        110        120
AASQPALWHTVTLSSPLVGRPAKGGVKAEKKLLASLEWLMPNRFSQLQRLTLIHWKSQVH

        130        140        150        160        170        180
PVLKLVGECCPRLTFLKLSGCHGVTADALVMLAKACCQLHSLDLQHSMVESTAVVSFLEE

        190        200        210        220        230        240
AGSRMRKLWLTYSSQTTAILGALLGSCCPQLQVLEVSTGINRNSIPLQLPVEALQKGCPQ

        250        260        270        280
LQVLRLLNLMWLPKPPGRGVAPGPGFPSLEELCLASSTCNFVS
```

FIG. 23A

```
         10        20        30        40        50        60
TGCGGCCGCGCCCGCACCCGCACCGGCACCCACGCCCACGCCCGAGGAAGGGCCCGACGCGGGCTGGGG

70       80        90        100       110       120       130
AGACCGCATTCCCTTGGAAATCCTGGTGCAGATTTTCGGGTTGTTGGTGGCGGCGGACGGCCCCATGCC

140      150       160       170       180       190       200
CTTCCTGGGCAGGGCTGCGCGCGTGTGCCGCCGCTGGCAGGAGGCCGCTTCCCAACCCGCGCTCTGGCA

210      220       230       240       250       260       270
CACCGTGACCCTGTCGTCCCCGCTGGTCGGCCGGCCTGCCAAGGGCGGGGTCAAGGCGGAGAAGAAGCT

280      290       300       310       320       330       340
CCTTGCTTCCCTGGAGTGGCTTATGCCCAATCGGTTTTCACAGCTCCAGAGGCTGACCCTCATCCACTG

 350      360       370       380       390       400       410
GAAGTCTCAGGTACACCCCGTGTTGAAGCTGGTAGGTGAGTGCTGTCCTCGGCTCACTTTCCTCAAGCT

  420      430       440       450       460       470       480
CTCCGGCTGCCACGGTGTGACTGCTGACGCTCTGGTCATGCTAGCCAAAGCCTGCTGCCAGCTCCATAG

   490      500       510       520       530       540       550
CCTGGACCTACAGCACTCCATGGTGGAGTCCACAGCTGTGGTGAGCTTCTTGGAGGAGGCAGGGTCCCG

    560      570       580       590       600       610       620
AATGCGCAAGTTGTGGCTGACCTACAGCTCCCAGACGACAGCCATCCTGGGCGCATTGCTGGGCAGCTG

     630      640       650       660       670       680       690
CTGCCCCCAGCTCCAGGTCCTGGAGGTGAGCACCGGCATCAACCGTAATAGCATTCCCCTTCAGCTGCC

      700      710       720       730       740       750
TGTCGAGGCTCTGCAGAAAGGCTGCCCTCAGCTCCAGGTGCTGCGGCTGTTGAACCTGATGTGGCTGCC

760        770       780       790       800       810       820
CAAGCCTCCGGGACGAGGGGTGGCTCCCGGACCAGGCTTCCCTAGCCTAGAGGAGCTCTGCCTGGCGAG

830      840       850
CTCAACCTGCAACTTTGTGAGC
```

FIG. 23B

```
         10        20        30        40        50        60
QHCSQKDTAELLRGLSLWNHAEERQKFFKYSVDEKSDKEAEVSEHSTGITHLPPEVMLSI

         70        80        90       100       110       120
FSYLNPQELCRCSQVSMKWSQLTKTGSLWKHLYPVHWARGDWYSGPATELDTEPDDEWVK

        130       140       150       160       170       180
NRKDESRAFHEWDEDADIDESEESAEESIAISIAQMEKRLLHGLIHNVLPYVGTSVKTLV

        190       200       210       220       230       240
LAYSSAVSSKMVRQILELCPNLEHLDLTQTDISDSAFDSWSWLGCCQSLRHLDLSGCEKI

        250       260       270       280       290       300
TDVALEKISRALGILTSHQSGFLKTSTSKITSTAWKNKDITMQSTKQYACLHDLTNKGIG

        310       320       330       340       350       360
EEIDNEHPWTKPVSSENFTSPYVWMLDAEDLADIEDTVEWRHRNVESLCVMETASNFSCS

        370       380       390       400       410       420
TSGCFSKDIVGLRTSVCWQQHCASPAFAYCGHSFCCTGTALRTMSSLPESSAMCRKAART

        430       440       450       460       470       480
RLPRGKDLIYFGSEKSDQETGRVLLFLSLSGCYQITDHGLRVLTLGGGLPYLEHLNLSGC

        490       500       510       520       530       540
LTITGAGLQDLVSACPSLNDEYFYYCDNINGPHADTASGCQNLQCGFRACCRSGE*PLTS

        550       560       570       580       590
DLCLLHLAEQAFFHALYS*HISCVNHPFLSVTCFGPIXYNFRNLNYQXIVML
```

FIG. 24A

```
      10        20        30        40        50        60        70        80        90
ACAACACTGCTCTCAGAAGGATACTGCAGAACTCCTTAGAGGTCTTAGCCTATGGAATCATGCTGAAGAGCGACAGAARTTTTTTAAATATTCC

    100       110       120       130       140       150       160       170       180
GTGGATGAAAAGTCAGATAAAGAAGCAGAAGTGTCAGAACACTCCACAGGTATAACCCATCTTCCTCCTGAGGTAATGCTGTCAATTTTCAGCT

 190       200       210       220       230       240       250       260       270       280
ATCTTAATCCTCAAGAGTTATGTCGATGCAGTCAAGTAAGCATGAAATGGTCTCAGCTGACAAAAACGGGATCGCTTTGGAAACATCTTTACCC

      290       300       310       320       330       340       350       360       370
TGTTCATTGGGCCAGAGGTGACTGGTATAGTGGTCCCGCAACTGAACTTGATACTGAACCTGATGATGAATGGGTGAAAAATAGGAAAGATGAA

  380       390       400       410       420       430       440       450       460       470
AGTCGTGCTTTTCATGAGTGGGATGAAGATGCTGACATTGATGAATCTGAAGAGTCTGCGGAGGAATCAATTGCTATCAGCATTGCACAAATGG

        480       490       500       510       520       530       540       550       560
AAAAACGTTTACTCCATGGCTTAATTCATAACGTTCTACCATATGTTGGTACTTCTGTAAAAACCTTAGTATTAGCATACAGCTCTGCAGTTTC

    570       580       590       600       610       620       630       640       650
CAGCAAAATGGTTAGGCAGATTTTAGAGCTTTGTCCTAACCTGGAGCATCTGGATCTTACCCAGACTGACATTTCAGATTCTGCATTTGACAGT

 660       670       680       690       700       710       720       730       740       750
TGGTCTTGGCTTGGTTGCTGCCAGAGTCTTCGGCATCTTGATCTGTCTGGTTGTGAGAAAATCACAGATGTGGCCCTAGAGAAGATTTCCAGAG

      760       770       780       790       800       810       820       830       840
CTCTTGGAATTCTGACATCTCATCAAAGTGGCTTTTTGAAAACATCTACAAGCAAAATTACTTCAACTGCGTGGAAAAATAAAGACATTACCAT

  850       860       870       880       890       900       910       920       930       940
GCAGTCCACCAAGCAGTATGCCTGTTTGCACGATTTAACTAACAAGGGCATTGGAGAAGAAATAGATAATGAACACCCCTGGACTAAGCCTGTT

        950       960       970       980       990      1000      1010      1020      1030
TCTTCTGAGAATTTCACTTCTCCTTATGTGTGGATGTTAGATGCTGAAGATTTGGCTGATATTGAAGATACTGTGGAATGGAGACATAGAAATG

   1040      1050      1060      1070      1080      1090      1100      1110      1120
TTGAAAGTCTTTGTGTAATGGAAACAGCATCCAACTTTAGTTGTTCCACCTCTGGTTGTTTTAGTAAGGACATTGTTGGACTAAGGACTAGTGT

1130      1140      1150      1160      1170      1180      1190      1200      1210      1220
CTGTTGGCAGCAGCATTGTGCTTCTCCAGCCTTTGCGTATTGTGGTCACTCATTTTGTTGTACAGGAACAGCTTTAAGAACTATGTCATCACTC

      1230      1240      1250      1260      1270      1280      1290      1300      1310
CCAGAATCTTCTGCAATGTGTAGAAAAGCAGCAAGGACTAGATTGCCTAGGGGAAAAGACTTAATTTACTTTGGGAGTGAAAAATCTGATCAAG

  1320      1330      1340      1350      1360      1370      1380      1390      1400      1410
AGACTGGACGTGTACTTCTGTTTCTCAGTTTATCTGGATGTTATCAGATCACAGACCATGGTCTCAGGGTTTTGACTCTGGGAGGAGGGCTGCC

        1420      1430      1440      1450      1460      1470      1480      1490      1500
TTATTTGGAGCACCTTAATCTCTCTGGTTGTCTTACTATAACTGGTGCAGGCCTGCAGGATTTGGTTTCAGCATGTCCTTCTCTGAATGATGAA

   1510      1520      1530      1540      1550      1560      1570      1580      1590
TACTTTTACTACTGTGACAACATTAACGGTCCTCATGCTGATACCGCCAGTGGATGCCAGAATTTGCAGTGTGGTTTTCGAGCCTGCTGCCGCT

1600      1610      1620      1630      1640      1650      1660      1670      1680      1690
CTGGCGAATGACCCTTGACTTCTGATCTTTGTCTACTTCATTTAGCTGAGCAGGCTTTCTTTCATGCACTTTACTCATAGCACATTTCTTGTGT

      1700      1710      1720      1730      1740      1750      1760      1770
TAACCATCCCTTTTTGAGCGTGACTTGTTTTGGGCCCATTNYTTACAACTTCAGAAATCTTAATTACCAGTGRATTGTAATGTTG
```

FIG. 24B

```
        10        20        30        40        50        60
RVTSGCGLARGSSAMVFSNNDEGLINKKLPKELLLRIFSFLDIVTLCRCAQISKAWNILA

        70        80        90       100       110       120
LDGSNWQRIDLFNFQIDVEGRVVENISKRCVGFLRKLSLRGCIGVGDSSLKTFAQNCRNI

       130       140       150       160       170       180
EHLNLNGCTKITDSTCYSLSRFCSKLKHLXLTSCVSITNSSLKGISEGCRNLEYLNLSWC

       190       200       210       220       230       240
DQITKDGIEALVRGCRGLKALLLRGCTQLEDEALKHIQNYCHELVSLNLQSCSRITDEGV

       250       260       270       280       290       300
VQICRGCHRLQALCLSGCSNLTDASLTALGLNCPRLQILEAARCSHLTDAGFTLLARNCH

       310       320       330       340       350       360
ELEKMDLEXCILITDSTLIQLSIHCPKLQALSLSHCELIXDDGILHLSNSTCGHERLRVL

       370       380       390       400       410       420
ELDNCLLITDVALXHLENCRGLERLELYDCQQVTRAGIKRMRAQLPHVKVHAYFAPVTPP

       430       440       450       460       470       480
TAVAGSGQRLCRCCVIL*QQLPGPKG**GILSSRRPESS*PTPPSPNLLILHWERHLQFP

       490       500       510       520       530       540
NRHLSRFKNGEDKKGFISNI*HHIVT*NMALT*LVLLLPSSLMSSLTSTHLLL*YL*RLI

       550
ILKTDQTGPASKYINCVQ*
```

FIG. 25A

```
         10         20         30         40         50         60         70         80         90
TTTTACTGTACACAGTTGATGTATTTTGATGCTGGGCCTGTCTGGTCTGTCTTGAGGATTATTAACCTTTAGAGGTATCAGAGAAGCAAATGGG
    100        110        120        130        140        150        160        170        180
TACTGGTGAGGCTGCTCATTAGGGAAGAGGGCAAAAGGAGCACTAGCTAGGTCAGAGCCATGTTTCAGGTCACAATGTGATGTCAGATGTTGCT
190        200        210        220        230        240        250        260        270        280
TATAAATCCTTTCTTGTCTTCGCCATTCTTAAATCTTGATAGGTGCCTGTTGGGAAACTGTAAATGCCTTTCCCAATGGAGAATCAACAGATTG
     290        300        310        320        330        340        350        360        370
GGTGATGGTGGAGTCGGTCAGGAAGACTCAGGTCTTCTAGAGGAAAGGATGCCTCATCACCCCTTNGGCCCAGGCAGCTGCTGTCAGAGAATGA
  380        390        400        410        420        430        440        450        460        470
CACAGCACCTGCACAGTCGCTGTCCACTTCCTGCCACTGCTGTCGGTGGGGTGACGGGAGCAAAGTAGGCGTGGACTTTGACATGAGGGAGCTG
       480        490        500        510        520        530        540        550        560
AGCCCGCATCCGCTTGATGCCTGCACGGGTAACCTGCTGGCAGTCGTACAGCTCGAGGCGCTCCAGGCCTCGGCAGTTCTCTAGGTGTYCCAGG
    570        580        590        600        610        620        630        640        650
GCCACATCAGTGATGAGGAGGCAGTTGTCCAACTCCAGTACCCGCAGCCTCTCATGGCCACAGGTACTGTTGCTCAGGTGCAGGATCCCATCAT
660        670        680        690        700        710        720        730        740        750
CTGKGATGAGTTCACAGTGGGACAGGCTCAGGGCTTGCAGTTTAGGACAGTGAATGGAGAGCTGGATGAGTGTGCTGTCGGTTATCAGGATGCA
     760        770        780        790        800        810        820        830        840
WTCTTCAAGATCCATCTTCTCCAATTCGTGGCAATTCCGAGCTAAAAGTGTAAAACCTGCGTCAGTCAAATGGGAGCATCGGGCAGCCTCCAAA
  850        860        870        880        890        900        910        920        930        940
ATTTGCAGTCGCGGACAGTTCAAACCCAGGGCTGTAAGAGAGGCATCTGTGAGGTTGCTGCAACCCGAAAGGCAGAGAGCCTGTAGCCGGTGAC
       950        960        970        980        990       1000       1010       1020       1030
AGCCCCTGCATATCTGCACCACACCTTCATCCGTGATACGTGAGCAGGACTGCAAGTTGAGGCTCACAAGCTCATGGCAGTAATTCTGAATGTG
   1040       1050       1060       1070       1080       1090       1100       1110       1120
TTTCAGAGCTTCATCTTCTAACTGTGTGCAGCCCCTCAGGAGCAGGGCTTTCAGGCCTCGACAACCTCGCACCAGTGCCTCGATGCCATCCTTC
1130       1140       1150       1160       1170       1180       1190       1200       1210       1220
GTGATCTGATCACACCAAGAGAGGTTCAGGTACTCCAGGTTTCGGCAGCCCTCACTGATCCCCTTCAAGGAGCTGTTTGTAATAGACACACAGG
    1230       1240       1250       1260       1270       1280       1290       1300       1310
AGGTCAGAWCCAGATGTTTCAGCTTGGAACAGAATCTGCTAAGGCTATAACACGTGCTGTCAGTGATTTTTGTGCATCCATTGAGGTTCAAATG
1320       1330       1340       1350       1360       1370       1380       1390       1400       1410
TTCAATGTTTCGGCAGTTCTGTGCAAAGGTCTTCAAGGAGGAATCCCCAACACCAATGCAGCCTCGCAAGCTGAGCTTCCTCAGGAATCCAACG
      1420       1430       1440       1450       1460       1470       1480       1490       1500
CATCGCTTCGAGATATTTTCCACCACTCGACCCTCTACATCTATTTGAAAGTTAAAAAGATCTATTCTTTGCCAGTTGCTTCCATCCAGGGCTA
   1510       1520       1530       1540       1550       1560       1570       1580       1590
AGATGTTCCAAGCCTTGGAAATCTGTGCACATCGGCACAAAGTTACTATATCCAAGAAGGAAAATATTCTTAACAGAAGTTCTTTGGGTAACTT
1600       1610       1620       1630       1640       1650       1660       1670       1680
TTTGTTAATAAGGCCTTCATCATTGTTTGAGAAAACCATGGCCGAAGAGCCGCGAGCGAGCCCACAGCCCGAAGTCACACGGC
```

FIG. 25B

```
        10        20        30        40        50        60
MSPVFPMLTVLTMFYYICLRRRARTATRGEMMNTHRAIESNSQTSPLNAEVVQYAKEVVD

        70        80        90       100       110       120
FSSHYGSENSMSYTMWNLAGVPNVFPSSGDFTQTAVFRTYGTWWDQCPSASLPFKRTPPN

       130       140       150       160       170       180
FQSQDYVELTFEQQVYPTAVHVLETYHPGAVIRILACSANPYSPNPPAEVRWEILWSERP

       190       200       210       220       230       240
TKVNASQARQFKPCIKQINFPTNLIRLEVNSSLLEYYTELDAVVLHGVKDKPVLSLKTSL

       250       260       270       280       290       300
IDMNDIEDDAYAEKDGCGMDSLNKKFSSAVLGEGPNNGYFDKLPYELIQLILNHLTLPDL

       310       320       330       340       350       360
CRLAQTCKLLSQHCCDPLQYIHLNLQPYWAKLDDTSLEFLQSRCTLVQWLNLSWTGNRGF

       370       380       390       400       410       420
ISVAGFSRFLKVCGSELVRLELSCSHFLNETCLEVISEMCPNLQALNLSSCDKLPPQAFN

       430       440       450       460       470       480
HIAKLCSLKRLVLYRTKVEQTALLSILNFCSELQHLSLGSCVMIEDYDVIASMIGAKCKK

       490       500       510       520       530       540
LRTLDLWRCKNITENGIAELASGCPLLEELDLGWCPTLQSSTGCFTRLAHQLPNLQKLFL

       550       560       570       580       590       600
TANRSVCDTDIDELACNCTRLQQLDILGTRMVSPASLRKLLESCKDLSLLDVSFCSQIDN

       610       620
RAVLELNASFPKVFIKKSFTQ
```

FIG. 26A

```
       10        20        30        40        50        60        70        80        90
ATGTCACCGGTCTTTCCCATGTTAACAGTTCTGACCATGTTTATTATATATGCCTTCGGCGCCGAGCCAGGACAGCTACAAGAGGAGAAATGA
      100       110       120       130       140       150       160       170       180
TGAACACCCATAGAGCTATAGAATCAAACAGCCAGACTTCCCCTCTCAATGCAGAGGTAGTCCAGTATGCCAAAGAAGTAGTGGATTTCAGTTC
190       200       210       220       230       240       250       260       270       280
CCATTATGGAAGTGAGAATAGTATGTCCTATACTATGTGGAATTTGGCTGGTGTACCAAATGTATTCCCAAGTTCTGGTGACTTTACTCAGACA
      290       300       310       320       330       340       350       360       370
GCTGTGTTTCGAACTTATGGGACATGGTGGGATCAGTGTCCTAGTGCTTCCTTGCCATTCAAGAGGACGCCACCTAATTTTCAGAGCCAGGACT
380       390       400       410       420       430       440       450       460       470
ATGTGGAACTTACTTTTGAACAACAGGTGTATCCTACAGCTGTACATGTTCTAGAAACCTATCATCCCGGAGCAGTCATTAGAATTCTCGCTTG
      480       490       500       510       520       530       540       550       560
TTCTGCAAATCCTTATTCCCCAAATCCACCAGCTGAAGTAAGATGGGAGATTCTTTGGTCAGAGAGACCTACGAAGGTGAATGCTTCCCAAGCT
      570       580       590       600       610       620       630       640       650
CGCCAGTTTAAACCTTGTATTAAGCAGATAAATTTCCCCACAAATCTTATACGACTGGAAGTAAATAGTTCTCTTCTGGAATATTACACTGAAT
660       670       680       690       700       710       720       730       740       750
TAGATGCAGTTGTGCTACATGGTGTGAAGGACAAGCCAGTGCTTTCTCTCAAGACTTCACTTATTGACATGAATGATATAGAAGATGATGCCTA
      760       770       780       790       800       810       820       830       840
TGCAGAAAAGGATGGTTGTGGAATGGACAGTCTTAACAAAAAGTTTAGCAGTGCTGTCCTCGGGGAAGGGCCAAATAATGGGTATTTTGATAAA
850       860       870       880       890       900       910       920       930       940
CTACCTTATGAGCTTATTCAGCTGATTCTGAATCATCTTACACTACCAGACCTGTGTAGATTAGCACAGACTTGCAAACTACTGAGCCAGCATT
      950       960       970       980       990      1000      1010      1020      1030
GCTGTGATCCTCTGCAATACATCCACCTCAATCTGCAACCATACTGGGCAAAACTAGATGACACTTCTCTGGAATTTCTACAGTCTCGCTGCAC
     1040      1050      1060      1070      1080      1090      1100      1110      1120
TCTTGTCCAGTGGCTTAATTTATCTTGGACTGGCAATAGAGGCTTCATCTCTGTTGCAGGATTTAGCAGGTTTCTGAAGGTTTGTGGATCCGAA
1130      1140      1150      1160      1170      1180      1190      1200      1210      1220
TTAGTACGCCTTGAATTGTCTTGCAGCCACTTTCTTAATGAAACTTGCTTAGAAGTTATTTCTGAGATGTGTCCAAATCTACAGGCCTTAAATC
     1230      1240      1250      1260      1270      1280      1290      1300      1310
TCTCCTCCTGTGATAAGCTACCACCTCAAGCTTTCAACCACATTGCCAAGTTATGCAGCCTTAAACGACTTGTTCTCTATCGAACAAAAGTAGA
1320      1330      1340      1350      1360      1370      1380      1390      1400      1410
GCAAACAGCACTGCTCAGCATTTTGAACTTCTGTTCAGAGCTTCAGCACCTCAGTTTAGGCAGTTGTGTCATGATTGAAGACTATGATGTGATA
     1420      1430      1440      1450      1460      1470      1480      1490      1500
GCTAGCATGATAGGAGCCAAGTGTAAAAAACTCCGGACCCTGGATCTGTGGAGATGTAAGAATATTACTGAGAATGGAATAGCAGAACTGGCTT
     1510      1520      1530      1540      1550      1560      1570      1580      1590
CTGGGTGTCCACTACTGGAGGAGCTTGACCTTGGCTGGTGCCCAACTCTGCAGAGCAGCACCGGGTGCTTCACCAGACTGGCACACCAGCTCCC
1600      1610      1620      1630      1640      1650      1660      1670      1680      1690
AAACTTGCAAAAACTCTTTCTTACAGCTAATAGATCTGTGTGTGACACAGACATTGATGAATTGGCATGTAATTGTACCAGGTTACAGCAGCTG
     1700      1710      1720      1730      1740      1750      1760      1770      1780
GACATATTAGGAACAAGAATGGTAAGTCCGGCATCCTTAAGAAAACTCCTGGAATCTTGTAAAGATCTTTCTTTACTTGATGTGTCCTTCTGTT
1790      1800      1810      1820      1830      1840      1850      1860
CGCAGATTGATAACAGAGCTGTGCTAGAACTGAATGCAAGCTTTCCAAAAGTGTTCATAAAAAAGAGCTTTACTCAGTGA
```

FIG. 26B

```
         10        20        30        40        50        60
MQLVPDIEFKITYTRSPDGDGVGNSYIEDNDDDSKMADLLSYFQQQLTFQESVLKLCQPE

         70        80        90       100       110       120
LESSQIHISVLPMEVLMYIFRWVVSSDLDLRSLEQLSLVCRGFYICARDPEIWRLACLKV

        130       140       150       160       170       180
WGRSCIKLVPYTSWREMFLERPRVRFDGVYISKTTYIRQGEQSLDGFYRAWHQVEYYRYI

        190       200       210       220       230       240
RFFPDGHVMMLTTPEEPQSIVPRLRTRNTRTDAILLGHYRLSQDTDNQTKVFAVITKKKE

        250       260       270       280       290       300
EKPLDYKYRYFRRVPVQEADQSFHVGLQLCSSGHQRFNKLIWIHHSCHITYKSTGETAVS

        310       320
AFEIDKMYTPLFFARVRSYTAFSERPL
```

FIG. 27A

```
        10        20        30        40        50        60
ATGCAACTTGTACCTGATATAGAGTTCAAGATTACTTATACCCGGTCTCCAGATGGTGATGGCGTTGGA

70        80        90       100       110       120       130
AACAGCTACATTGAAGATAATGATGATGACAGCAAAATGGCAGATCTCTTGTCCTACTTCCAGCAGCAA

140       150       160       170       180       190       200
CTCACATTTCAGGAGTCTGTGCTTAAACTGTGTCAGCCTGAGCTTGAGAGCAGTCAGATTCACATATCA

210       220       230       240       250       260       270
GTGCTGCCAATGGAGGTCCTGATGTACATCTTCCGATGGGTGGTGTCTAGTGACTTGGACCTCAGATCA

 280       290       300       310       320       330       340
TTGGAGCAGTTGTCGCTGGTGTGCAGAGGATTCTACATCTGTGCCAGAGACCCTGAAATATGGCGTCTG

  350       360       370       380       390       400       410
GCCTGCTTGAAAGTTTGGGGCAGAAGCTGTATTAAACTTGTTCCGTACACGTCCTGGAGAGAGATGTTT

   420       430       440       450       460       470       480
TTAGAACGGCCTCGTGTTCGGTTTGATGGCGTGTATATCAGTAAAACCACATATATTCGTCAAGGGGAA

    490       500       510       520       530       540       550
CAGTCTCTTGATGGTTTCTATAGAGCCTGGCACCAAGTGGAATATTACAGGTACATAAGATTCTTTCCT

     560       570       580       590       600       610       620
GATGGCCATGTGATGATGTTGACAACCCCTGAAGAGCCTCAGTCCATTGTTCCACGTTTAAGAACTAGG

      630       640       650       660       670       680       690
AATACCAGGACTGATGCAATTCTACTGGGTCACTATCGCTTGTCACAAGACACAGACAATCAGACCAAA

       700       710       720       730       740       750
GTATTTGCTGTAATAACTAAGAAAAAAGAAGAAAAACCACTTGACTATAAATACAGATATTTTCGTCGT

760       770       780       790       800       810       820
GTCCCTGTACAAGAAGCAGATCAGAGTTTTCATGTGGGGCTACAGCTATGTTCCAGTGGTCACCAGAGG

830       840       850       860       870       880       890
TTCAACAAACTCATCTGGATACATCATTCTTGTCACATTACTTACAAATCAACTGGTGAGACTGCAGTC

900       910       920       930       940       950       960
AGTGCTTTTGAGATTGACAAGATGTACACCCCCTTGTTCTTCGCCAGAGTAAGGAGCTACACAGCTTTC

 970       980
TCAGAAAGGCCTCTGTAG
```

FIG. 27B

```
       .10        20        30        40        50        60
AALDPDLENDDFFVRKTGAFHANPYVLRAFEDFRKFSEQDDSVERDIILQCREGELVLPD

        70        80        90       100       110       120
LEKDDMIVRRIPAQKKEVPLSGAPDRYHPVPFPEPWTLPPEIQAKFLCVLERTCPSKEKS

       130       140       150       160       170       180
NSCRILVPSYRQKKDDMLTRKIQSWKLGTTVPPISFTPGPCSEADLKRWEAIREASRLRH

       190       200       210       220       230       240
KKRLMVERLFQKIYGENGSKSMSDVSAEDVQNLRQLRYEEMQKIKSQLKEQDQKWQDDLA

       250
KWKDRRKSYTSDLQK
```

FIG. 28A

```
         10        20        30        40        50        60
GCAGCCCTGGATCCTGACTTAGAGAATGATGATTTCTTTGTCAGAAAGACTGGGGCTTTCCATGCAAAT

70        80        90        100       110       120       130
CCATATGTTCTCCGAGCTTTTGAAGACTTTAGAAAGTTCTCTGAGCAAGATGATTCTGTAGAGCGAGAT

140       150       160       170       180       190       200
ATAATTTTACAGTGTAGAGAAGGTGAACTTGTACTTCCGGATTTGGAAAAAGATGATATGATTGTTCGC

210       220       230       240       250       260       270
CGAATCCCAGCACAGAAGAAAGAAGTGCCGCTGTCTGGGGCCCCAGATAGATACCACCCAGTCCCTTTT

280       290       300       310       320       330       340
CCCGAACCCTGGACTCTTCCTCCAGAAATTCAAGCAAAATTTCTCTGTGTACTTGAAAGGACATGCCCA

350       360       370       380       390       400       410
TCCAAAGAAAAAAGTAATAGCTGTAGAATATTAGTTCCTTCATATCGGCAGAAGAAAGATGACATGCTG

420       430       440       450       460       470       480
ACACGTAAGATTCAGTCCTGGAAACTGGGAACTACCGTGCCTCCCATCAGTTTCACNCCTGGCCCCTGC

490       500       510       520       530       540       550
AGTGAGGCTGACTTGAAGAGATGGGAGGCCATCCGGGAGGCCAGCAGACTCAGGCACAAGAAAAGGCTG

560       570       580       590       600       610       620
ATGGTGGAGAGACTCTTTCAAAAGATTTATGGTGAGAATGGGAGTAAGTCCATGAGTGATGTCAGCGCA

630       640       650       660       670       680       690
GAAGATGTTCAAAACTTGCGTCAGCTGCGTTACGAGGAGATGCAGAAAATAAAATCACAATTAAAAGAA

700       710       720       730       740       750
CAAGATCAGAAATGGCAGGATGACCTTGCAAAATGGAAAGATCGTCGAAAAAGTTACACTTCAGATCTG

760
CAGAAG
```

FIG. 28B

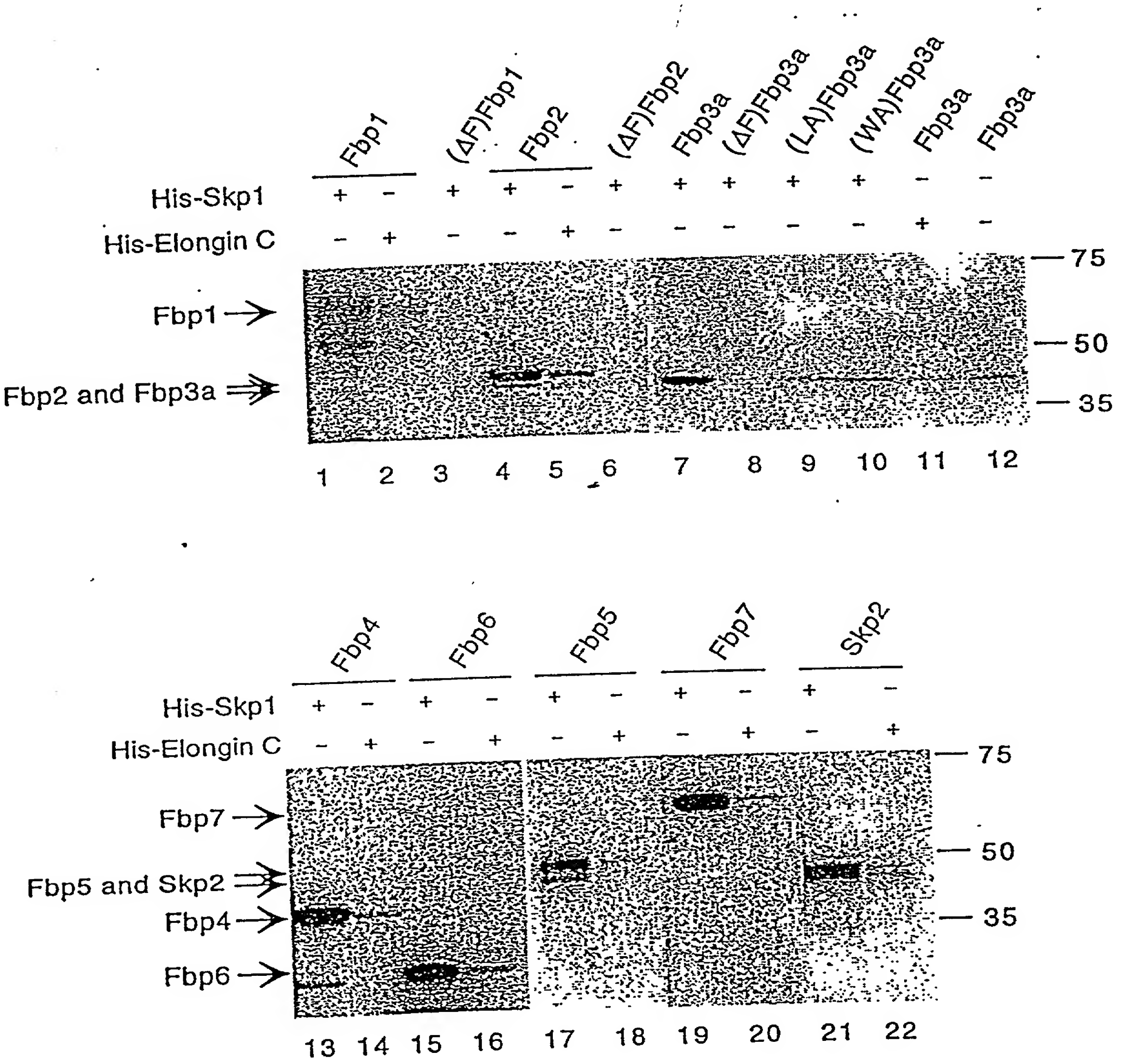
Fbp1
(ΔF)Fbp1
Fbp2
(ΔF)Fbp2
Fbp3a
(ΔF)Fbp3a
(LA)Fbp3a
(WA)Fbp3a
Fbp3a
Fbp3a
His-Skp1
+ − + + − + + + + + − −
His-Elongin C
− + − − + − − − − − + −
Fbp1
Fbp2 and Fbp3a
75
50
35
1 2 3 4 5 6 7 8 9 10 11 12
Fbp4
Fbp6
Fbp5
Fbp7
Skp2
His-Skp1
+ − + − + − + − + −
His-Elongin C
− + − + − + − + − +
Fbp7
Fbp5 and Skp2
Fbp4
Fbp6
75
50
35
13 14 15 16 17 18 19 20 21 22

FIG. 29

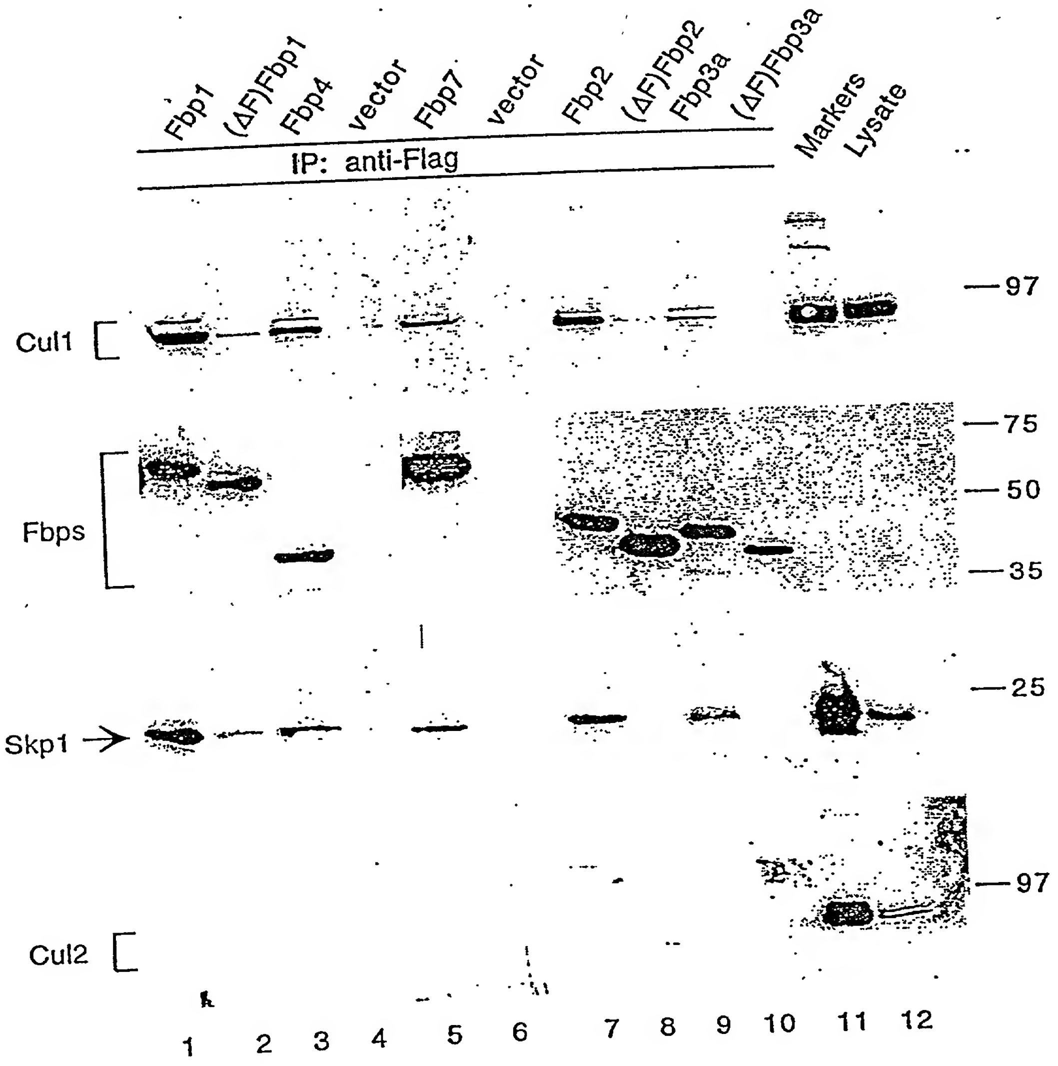
Fbp1
(ΔF)Fbp1
Fbp4
vector
Fbp7
vector
Fbp2
(ΔF)Fbp2
Fbp3a
(ΔF)Fbp3a
Markers
Lysate
IP: anti-Flag
Cul1
Fbps
Skp1
Cul2
97
75
50
35
25
97
1
2
3
4
5
6
7
8
9
10
11
12

FIG. 30

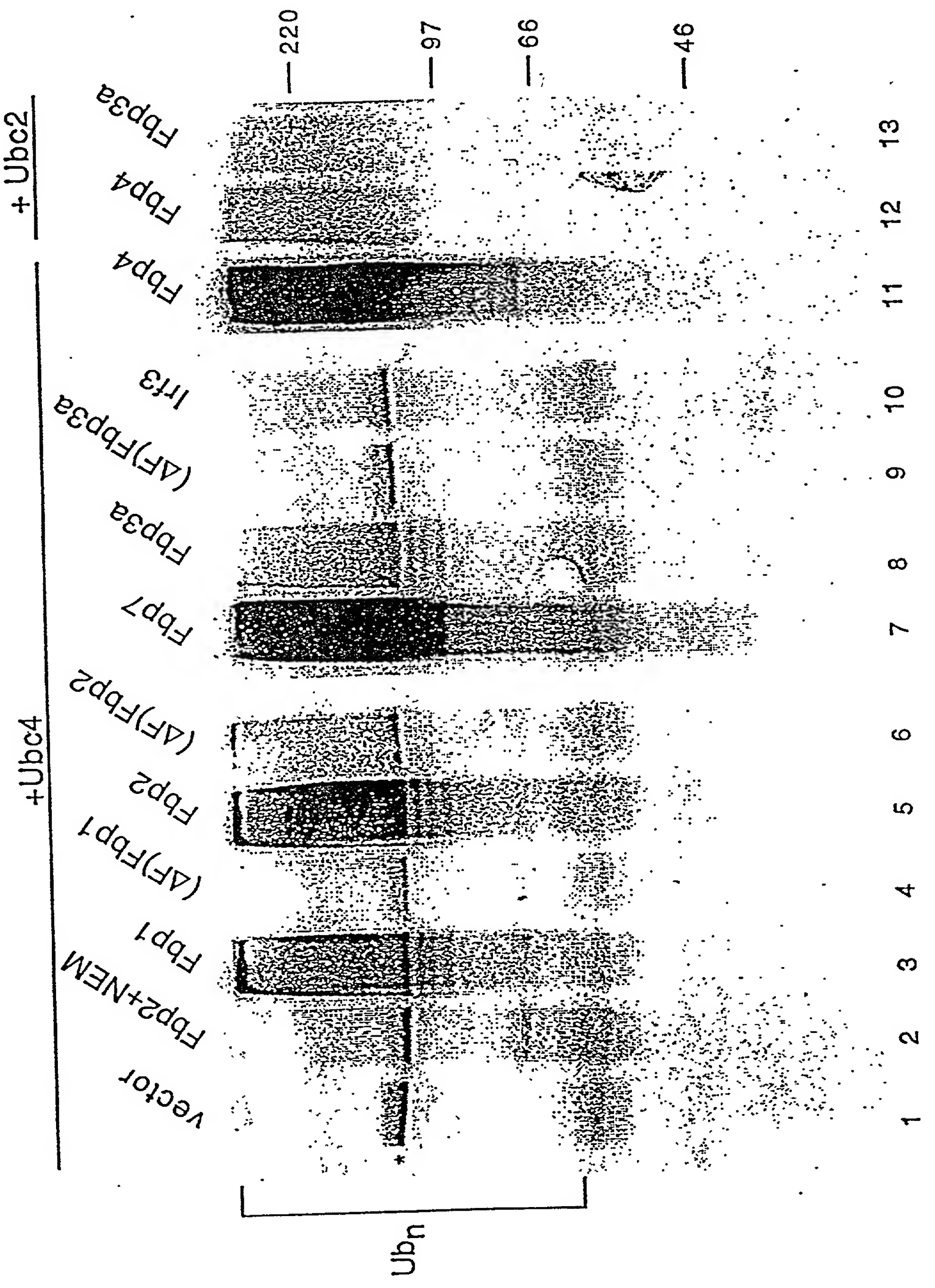
+Ubc4
+ Ubc2
vector
Fbp2+NEM
Fbp1
(ΔF)Fbp1
Fbp2
(ΔF)Fbp2
Fbp7
Fbp3a
(ΔF)Fbp3a
Irf3
Fbp4
Fbp4
Fbp3a
220
97
66
46
*
1
2
3
4
5
6
7
8
9
10
11
12
13
Ub$_n$

FIG. 31

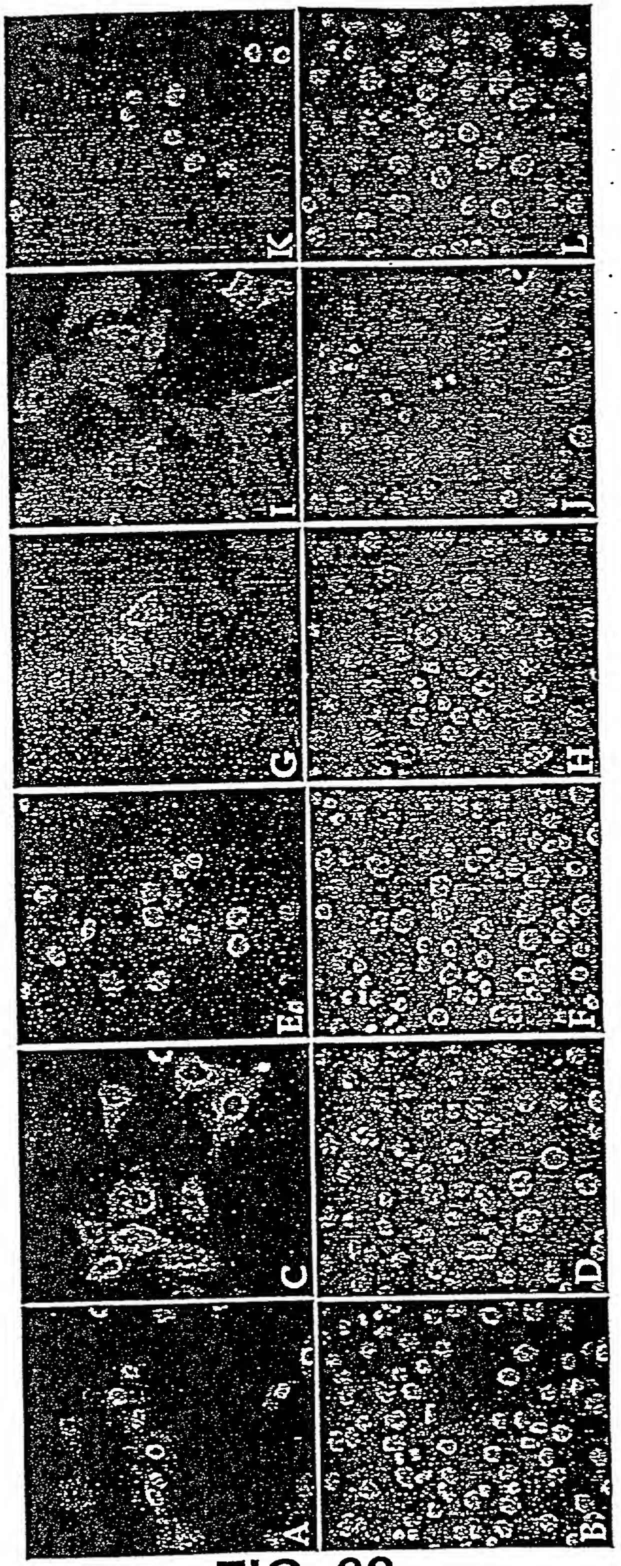

FIG. 32

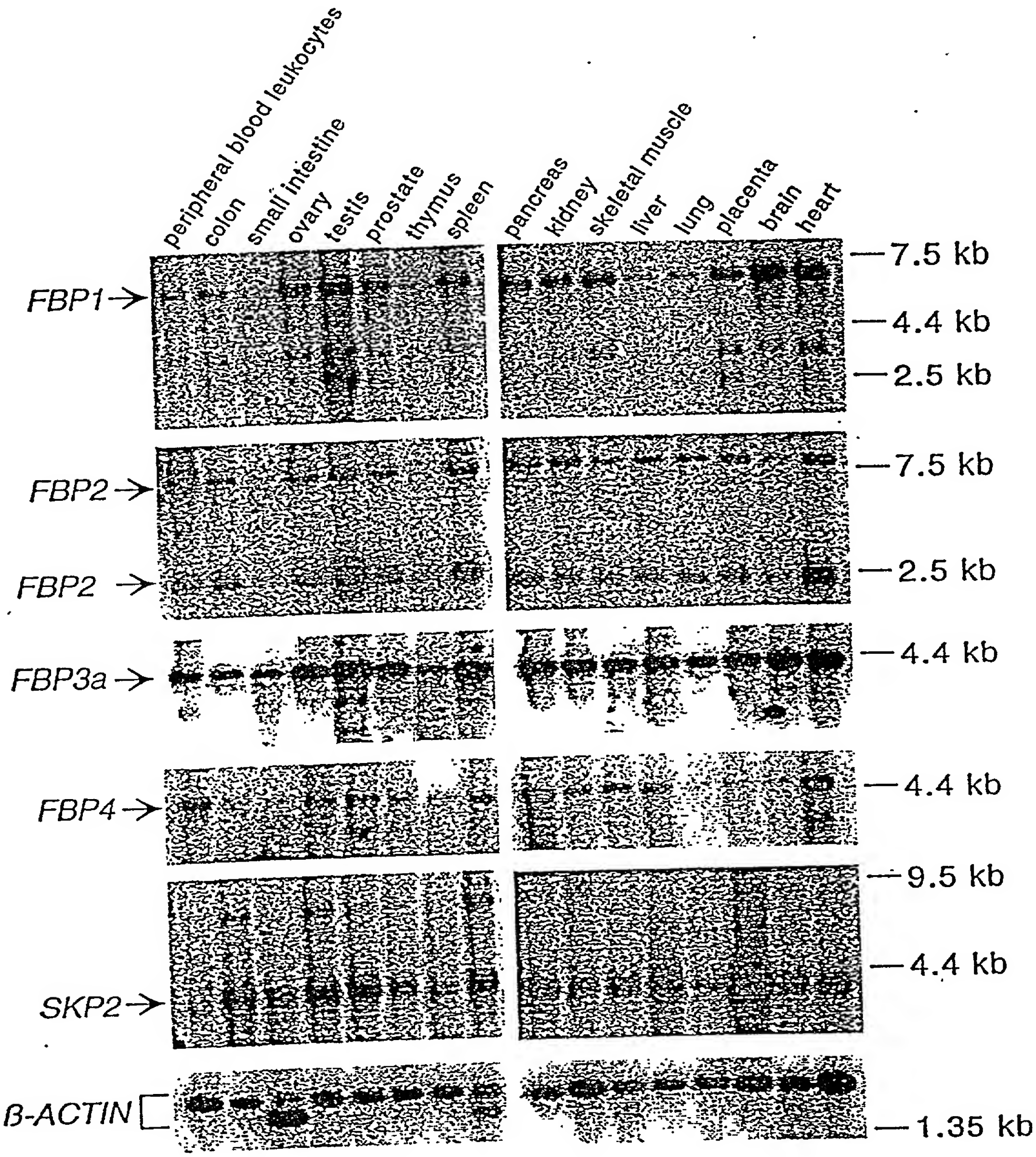
peripheral blood leukocytes
colon
small intestine
ovary
testis
prostate
thymus
spleen
pancreas
kidney
skeletal muscle
liver
lung
placenta
brain
heart
FBP1
FBP2
FBP2
FBP3a
FBP4
SKP2
β-ACTIN
7.5 kb
4.4 kb
2.5 kb
7.5 kb
2.5 kb
4.4 kb
4.4 kb
9.5 kb
4.4 kb
1.35 kb

FIG. 33

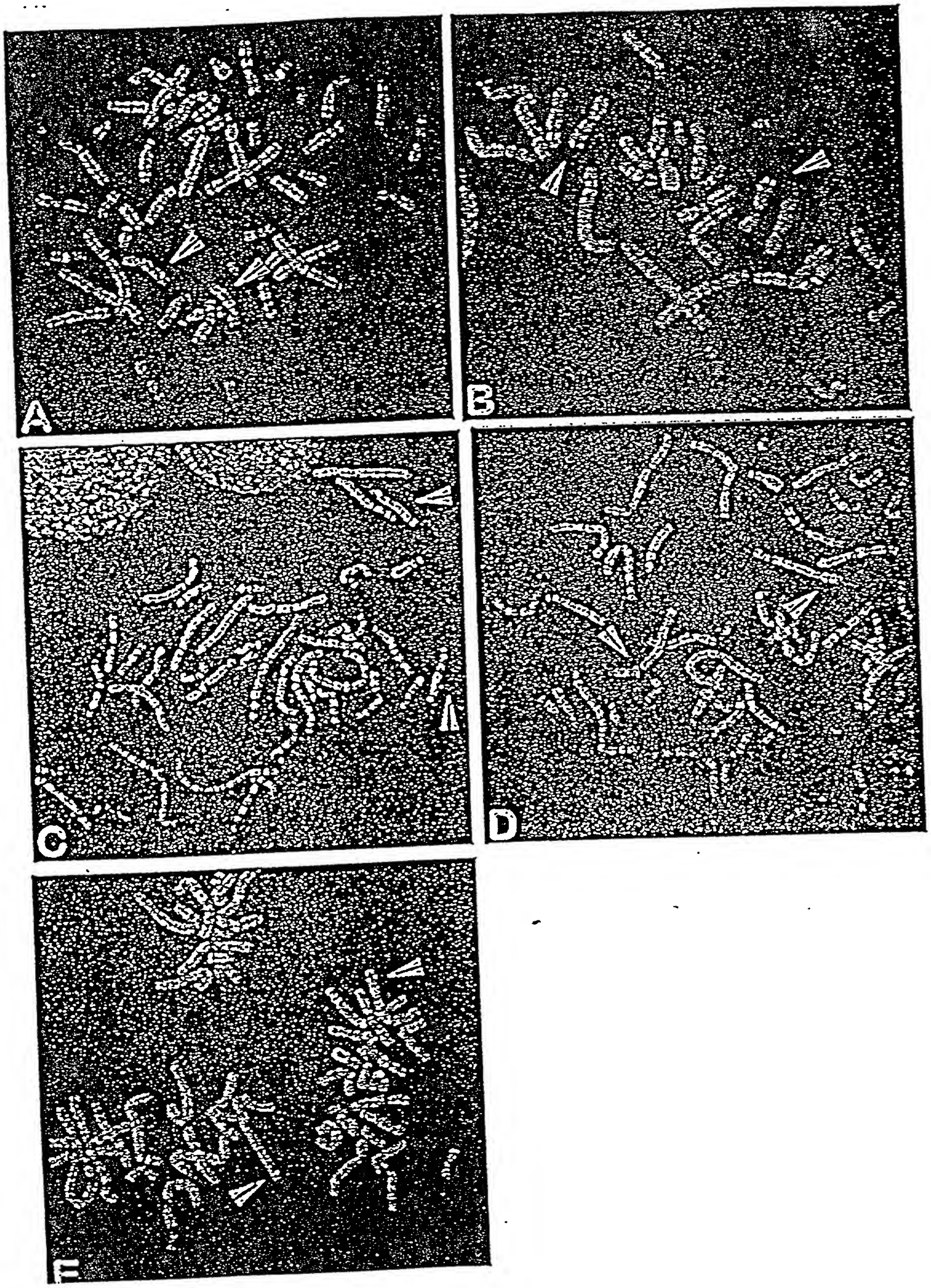

FIG. 34 A-E

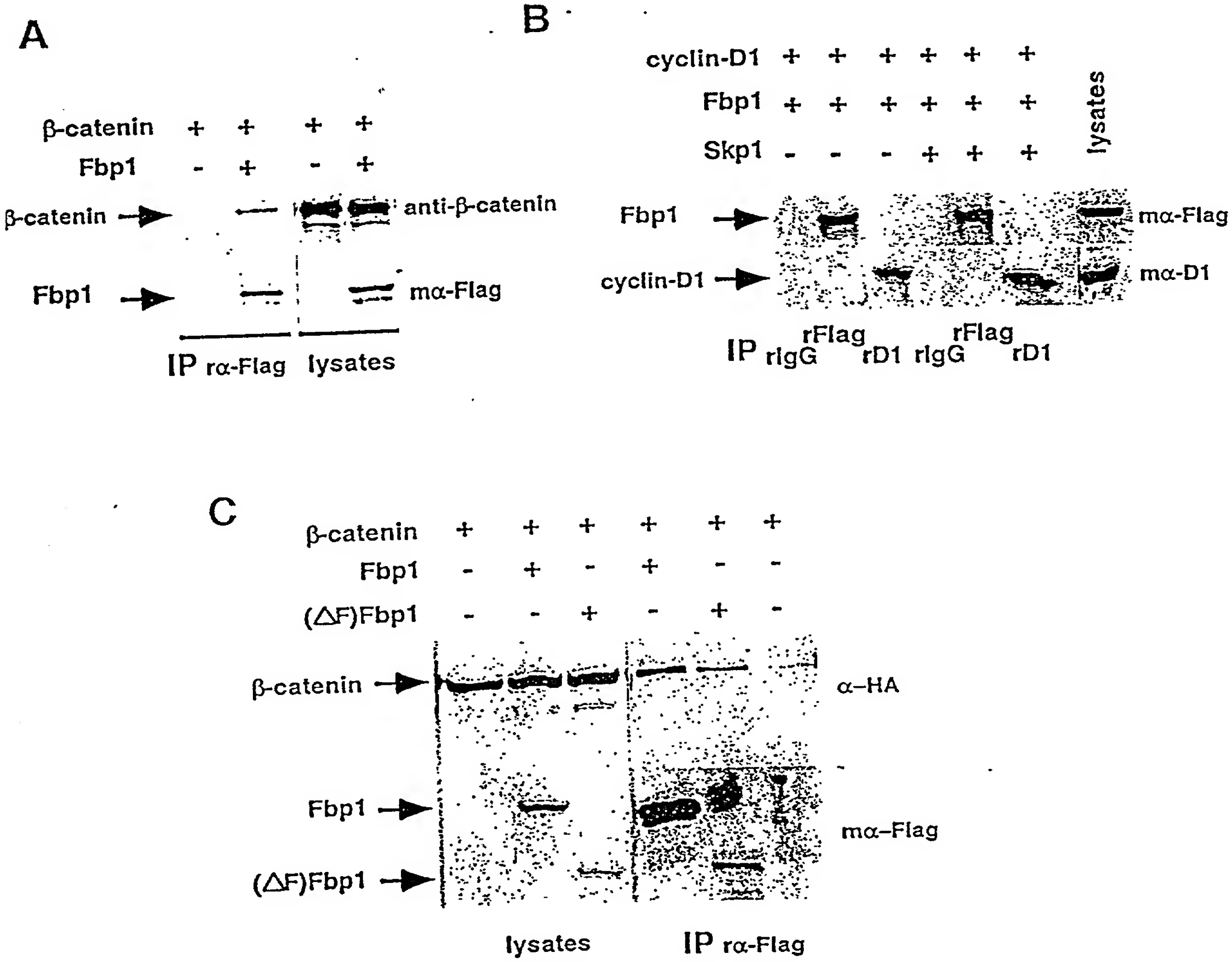
A
β-catenin + + + +
Fbp1 - + - +
β-catenin
anti-β-catenin
Fbp1
mα-Flag
IP rα-Flag
lysates
B
cyclin-D1 + + + + + +
Fbp1 + + + + + +
Skp1 - - - + + +
lysates
Fbp1
mα-Flag
cyclin-D1
mα-D1
IP rIgG rFlag rD1 rIgG rFlag rD1
C
β-catenin + + + + + +
Fbp1 - + - + - -
(ΔF)Fbp1 - - + - + -
β-catenin
α–HA
Fbp1
mα-Flag
(ΔF)Fbp1
lysates
IP rα-Flag

FIG. 35 A-C

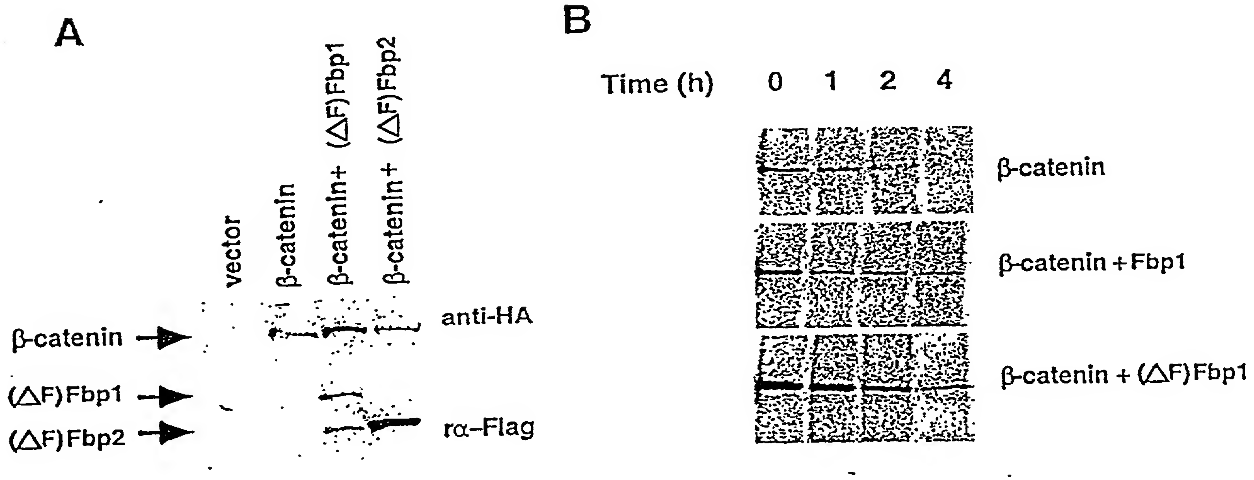
A
vector
β-catenin
β-catenin+ (ΔF)Fbp1
β-catenin+ (ΔF)Fbp2
β-catenin
(ΔF)Fbp1
(ΔF)Fbp2
anti-HA
rα-Flag
B
Time (h)
0
1
2
4
β-catenin
β-catenin + Fbp1
β-catenin + (ΔF)Fbp1

FIG. 36 A-B

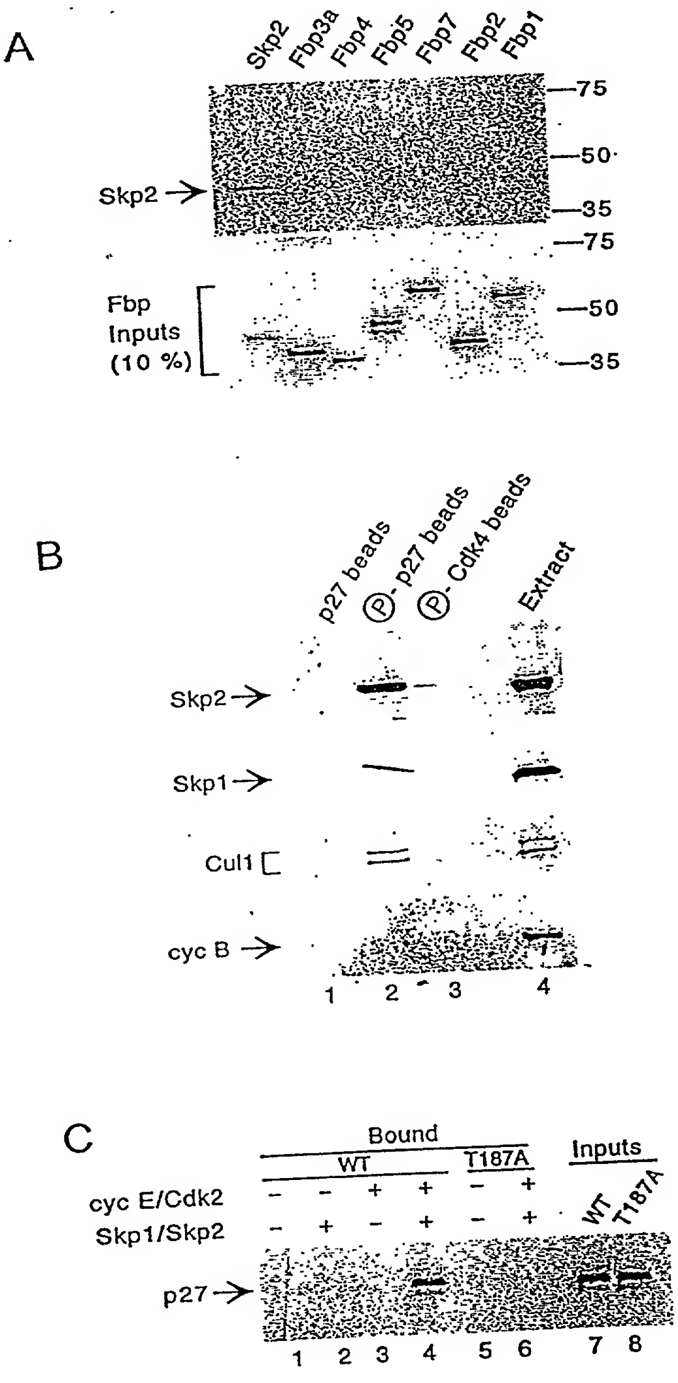
A
Skp2
Fbp3a
Fbp4
Fbp5
Fbp7
Fbp2
Fbp1
75
50
35
Skp2
75
Fbp Inputs (10 %)
50
35
B
p27 beads
Ⓟ-p27 beads
Ⓟ-Cdk4 beads
Extract
Skp2
Skp1
Cul1
cyc B
1
2
3
4
C
Bound
WT
T187A
Inputs
cyc E/Cdk2
Skp1/Skp2
– – + + – +
– + – + – +
WT
T187A
p27
1 2 3 4 5 6 7 8

FIG. 37 A-C

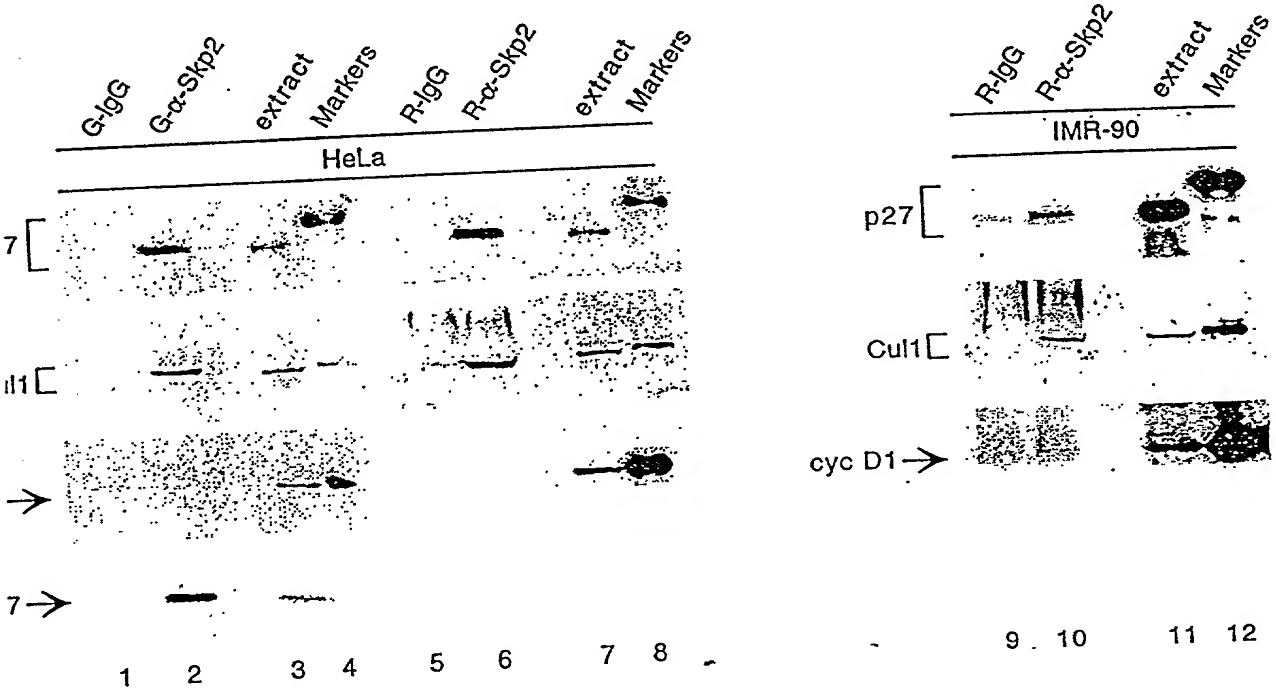
G-IgG
G-α-Skp2
extract
Markers
R-IgG
R-α-Skp2
extract
Markers
HeLa
7
ll1
7
R-IgG
R-α-Skp2
extract
Markers
IMR-90
p27
Cul1
cyc D1
1
2
3
4
5
6
7
8
9
10
11
12

FIG. 38

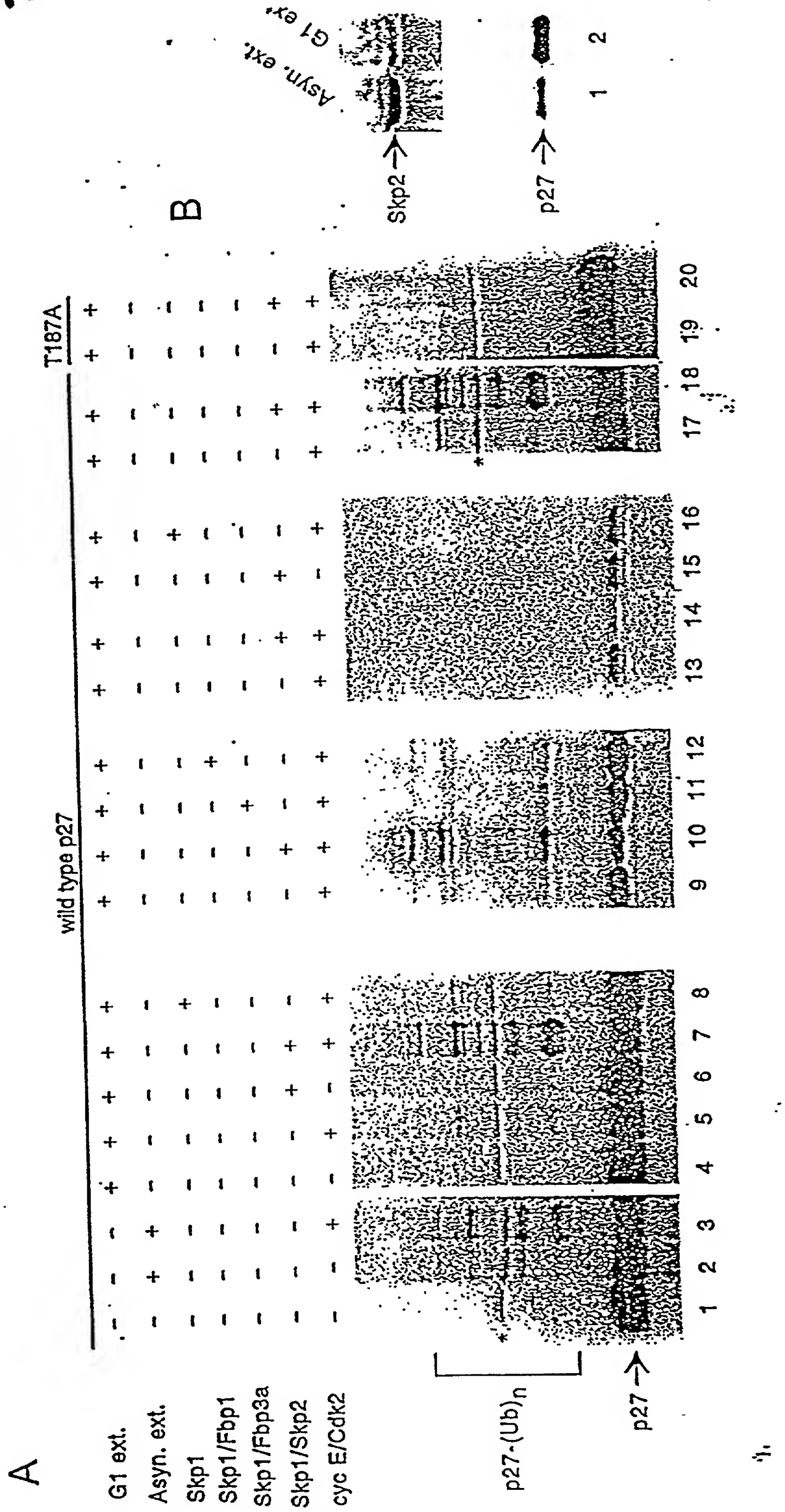
A
G1 ext.
Asyn. ext.
Skp1
Skp1/Fbp1
Skp1/Fbp3a
Skp1/Skp2
cyc E/Cdk2
wild type p27
T187A
p27-(Ub)n
p27
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
B
Asyn. ext.
G1 ex.
Skp2
p27
1 2

FIG. 39 A-B

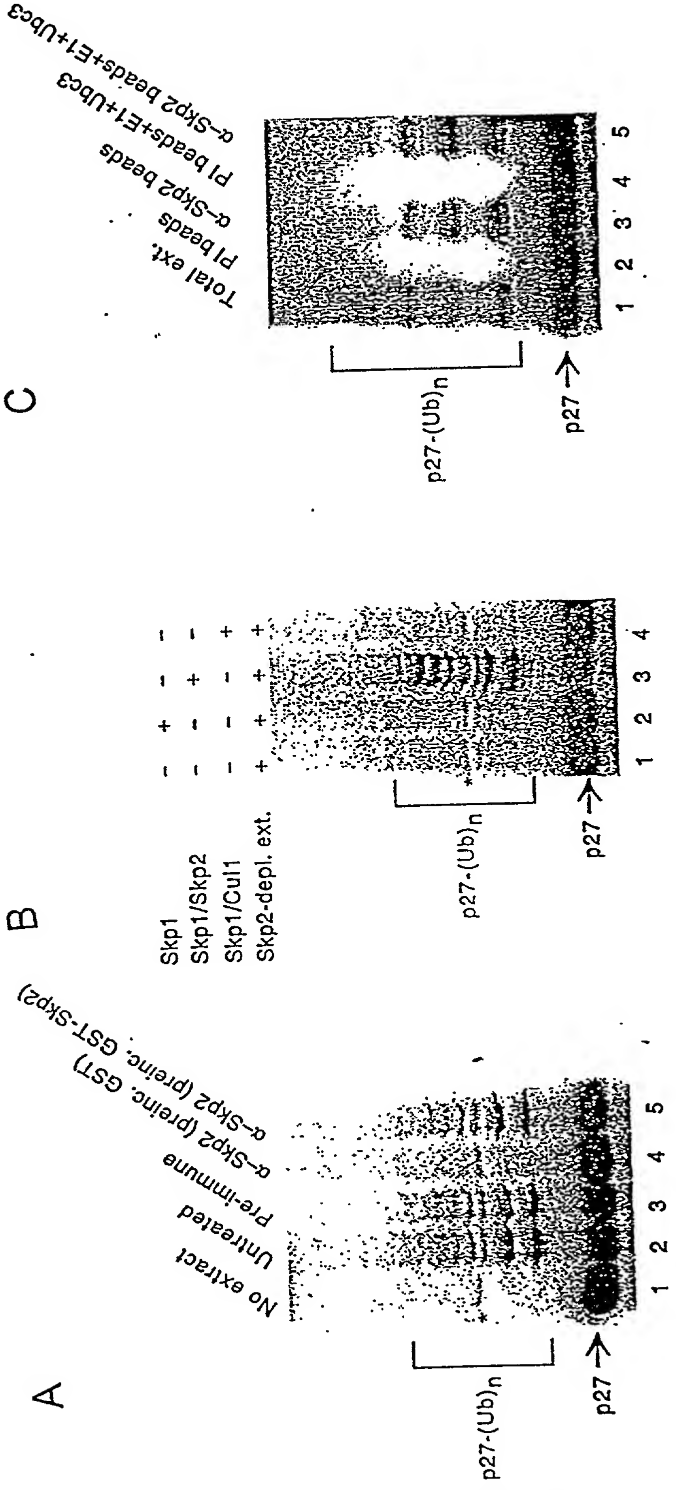
C
Total ext.
PI beads
α-Skp2 beads
PI beads+E1+Ubc3
α-Skp2 beads+E1+Ubc3
p27-(Ub)n
p27
1 2 3 4 5
B
Skp1
Skp1/Skp2
Skp1/Cul1
Skp2-depl. ext.
- + - -
- - + -
- - - +
+ + + +
p27-(Ub)n
p27
1 2 3 4
A
No extract
Untreated
Pre-immune
α-Skp2 (preinc. GST)
α-Skp2 (preinc. GST-Skp2)
p27-(Ub)n
p27
1 2 3 4 5

FIG. 40 A-C

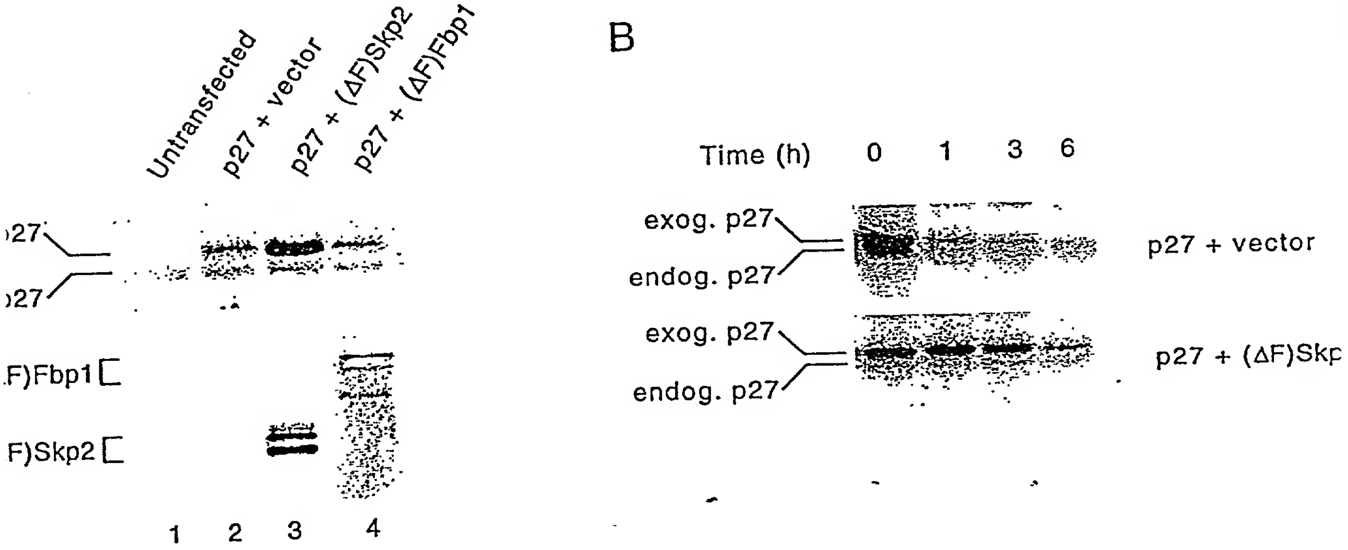
Untransfected
p27 + vector
p27 + (ΔF)Skp2
p27 + (ΔF)Fbp1
›27
›27
.F)Fbp1
.F)Skp2
1
2
3
4
B
Time (h)
0
1
3
6
exog. p27
endog. p27
p27 + vector
exog. p27
endog. p27
p27 + (ΔF)Skp

FIG. 41 A-B

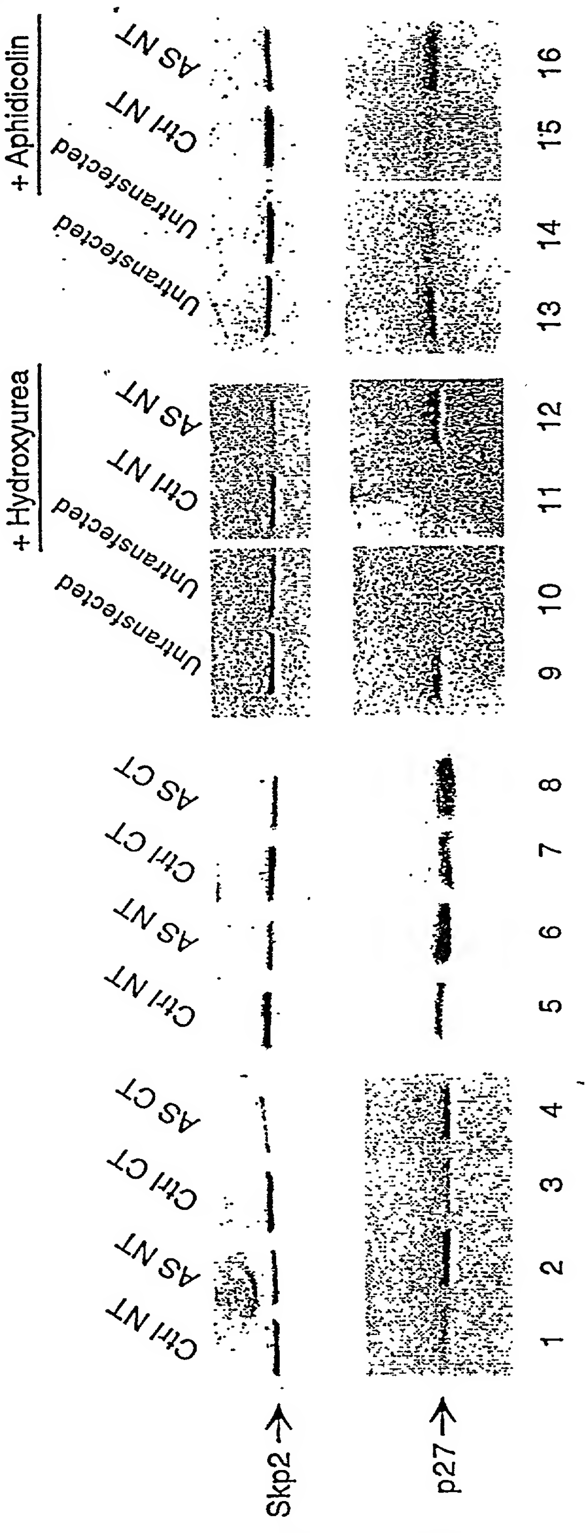
Skp2
p27
Ctrl NT
AS NT
Ctrl CT
AS CT
Ctrl NT
AS NT
Ctrl CT
AS CT
Untransfected
Untransfected
Ctrl NT
AS NT
+ Hydroxyurea
Untransfected
Untransfected
Ctrl NT
AS NT
+ Aphidicolin
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

FIG. 42

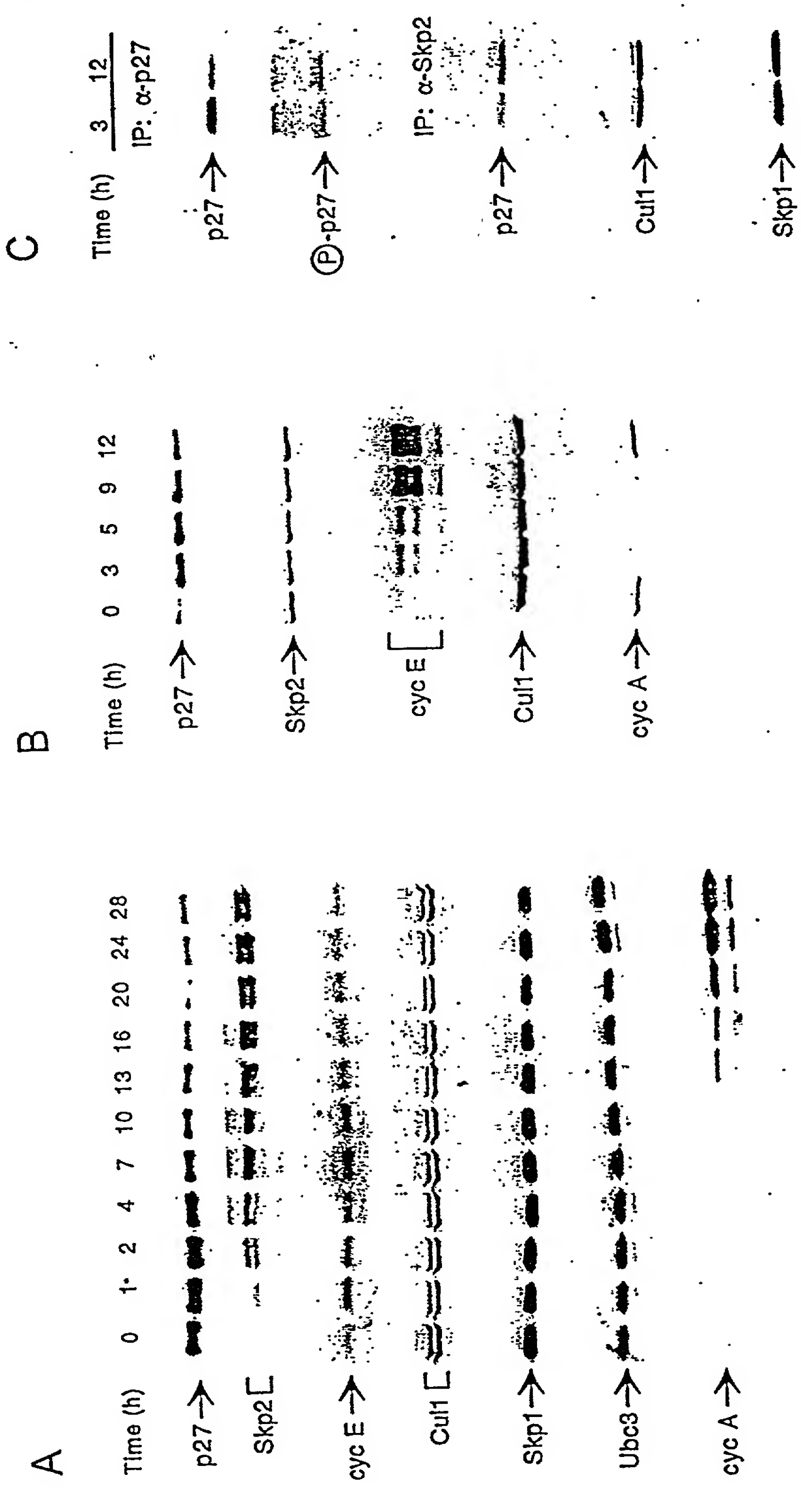
A
Time (h)
0
1
2
4
7
10
13
16
20
24
28
p27
Skp2
cyc E
Cul1
Skp1
Ubc3
cyc A
B
Time (h)
0
3
5
9
12
p27
Skp2
cyc E
Cul1
cyc A
C
Time (h)
3
12
IP: α-p27
p27
Ⓟ-p27
IP: α-Skp2
p27
Cul1
Skp1
1
2

FIG. 43 A-C

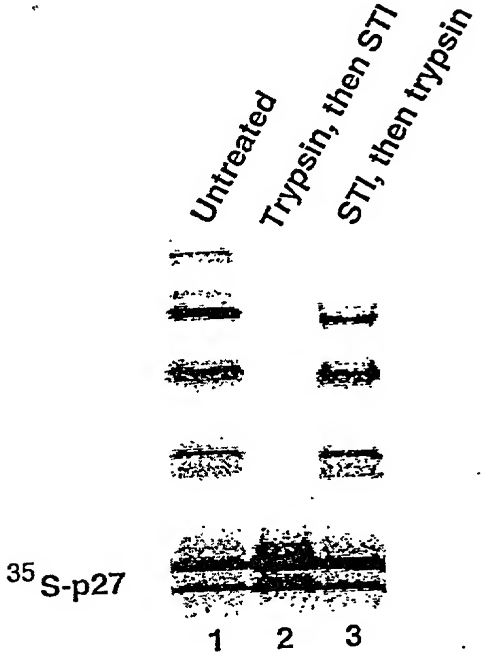

FIG. 44

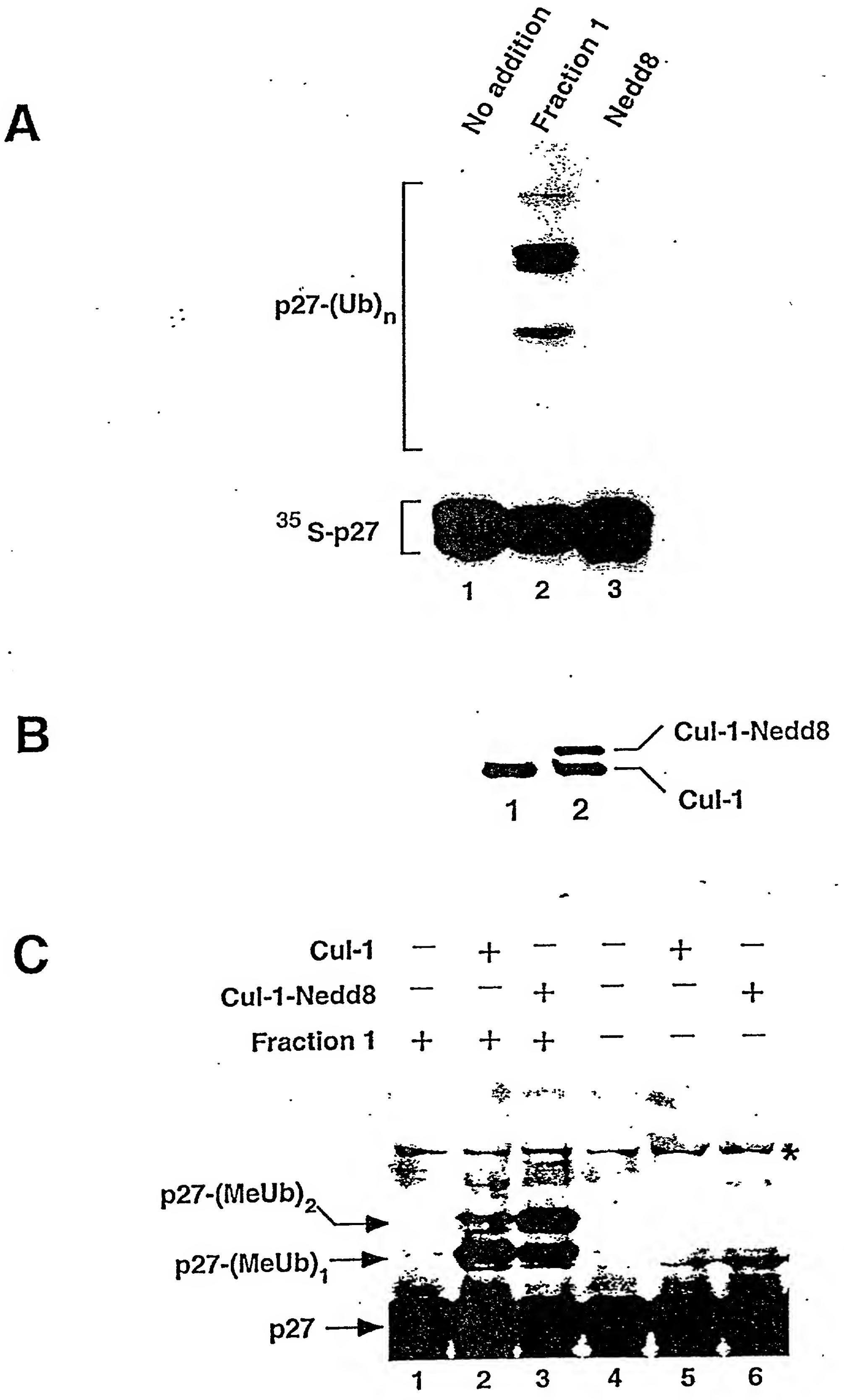
A
No addition
Fraction 1
Nedd8
p27-(Ub)$_n$
^{35}S-p27
1
2
3
B
Cul-1-Nedd8
Cul-1
1
2
C
Cul-1 − + − − + −
Cul-1-Nedd8 − − + − − +
Fraction 1 + + + − − −
*
p27-(MeUb)$_2$
p27-(MeUb)$_1$
p27
1
2
3
4
5
6

FIG. 45

914-090

(SHEET 72 OF 80

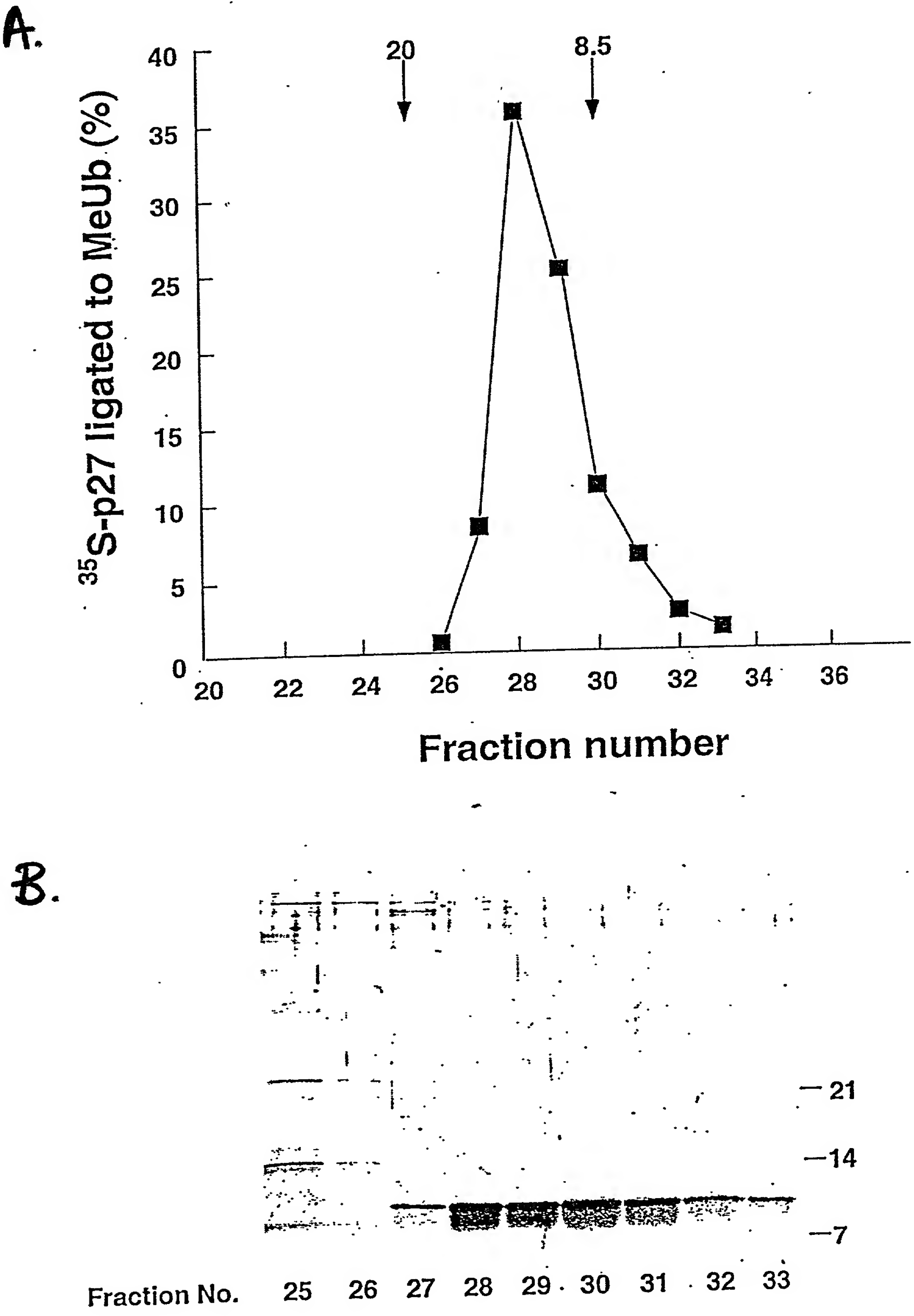

FIG. 46

114-090

(SHEET 73 OF 80)

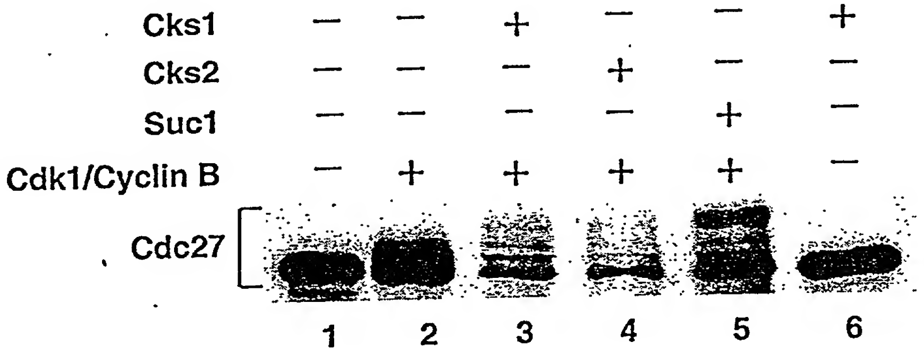

FIG. 47

914-090 (SHEET 74 OF 80)

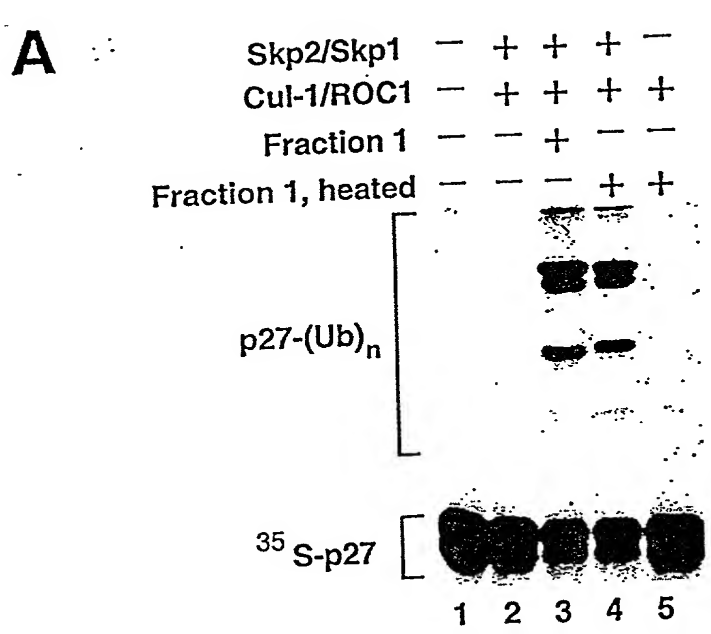

FIG. 48

5914-090

(SHEET 75 OF 80

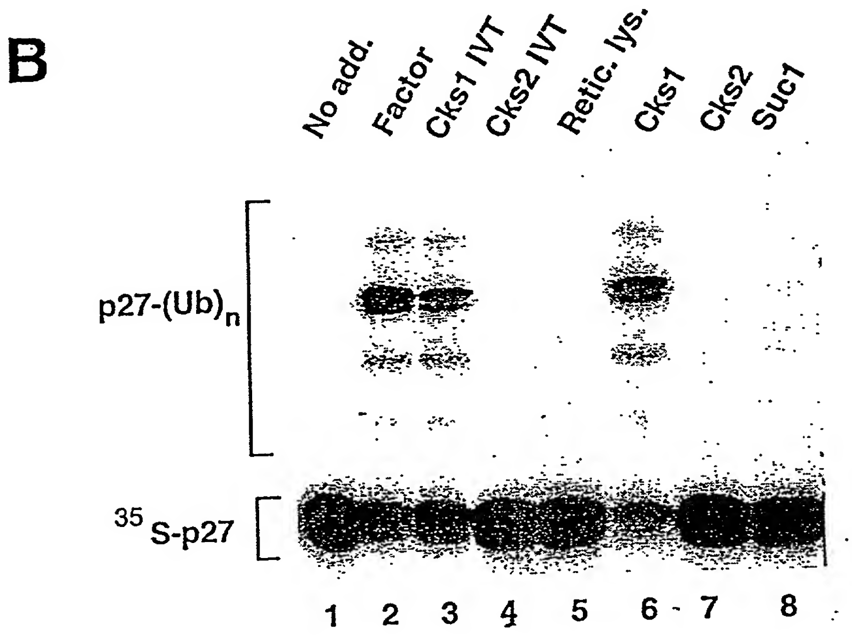

FIG. 48

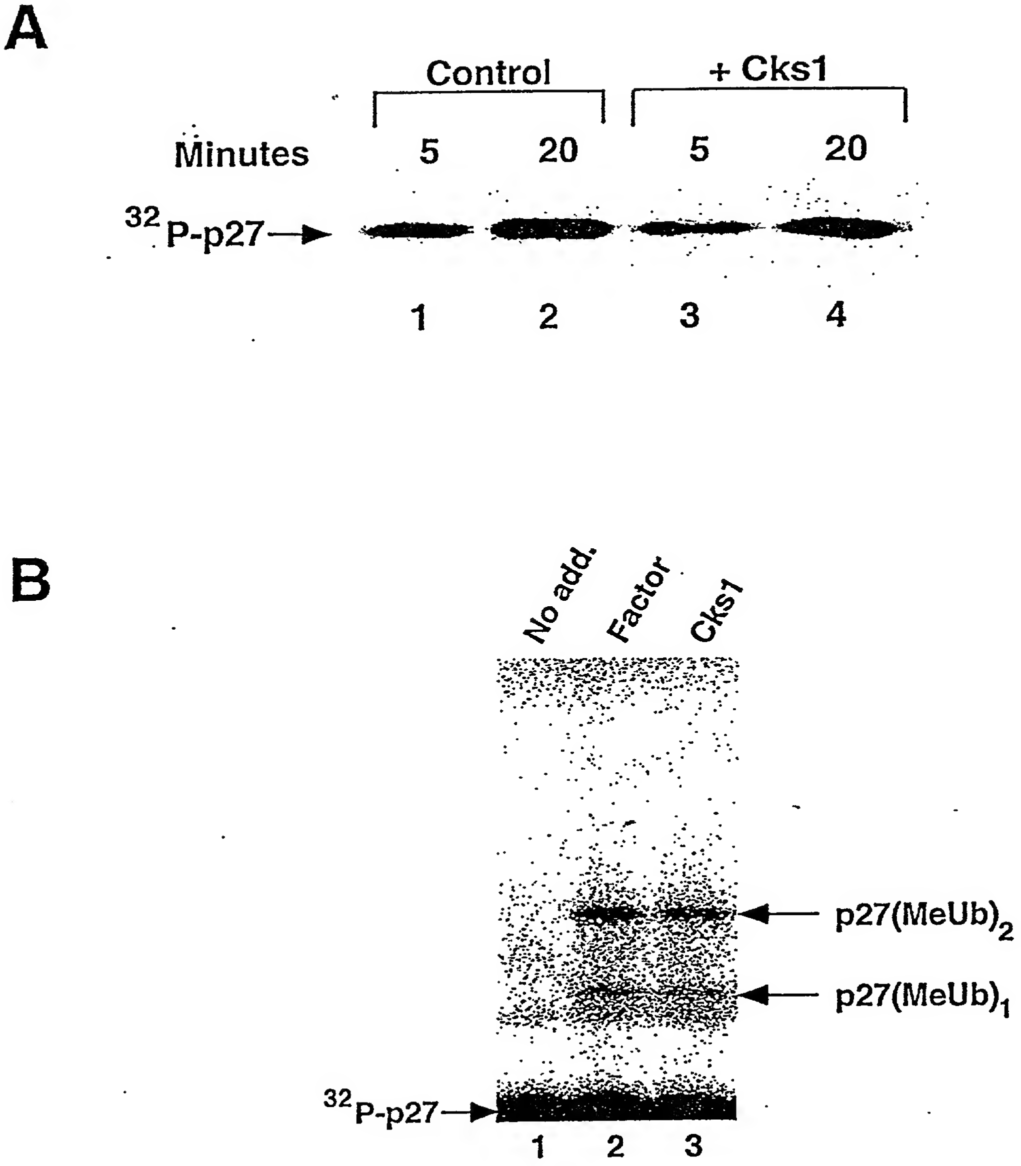
A
Control
+ Cks1
Minutes
5
20
5
20
^{32}P-p27
1
2
3
4
B
No add.
Factor
Cks1
p27(MeUb)$_2$
p27(MeUb)$_1$
^{32}P-p27
1
2
3

FIG. 49

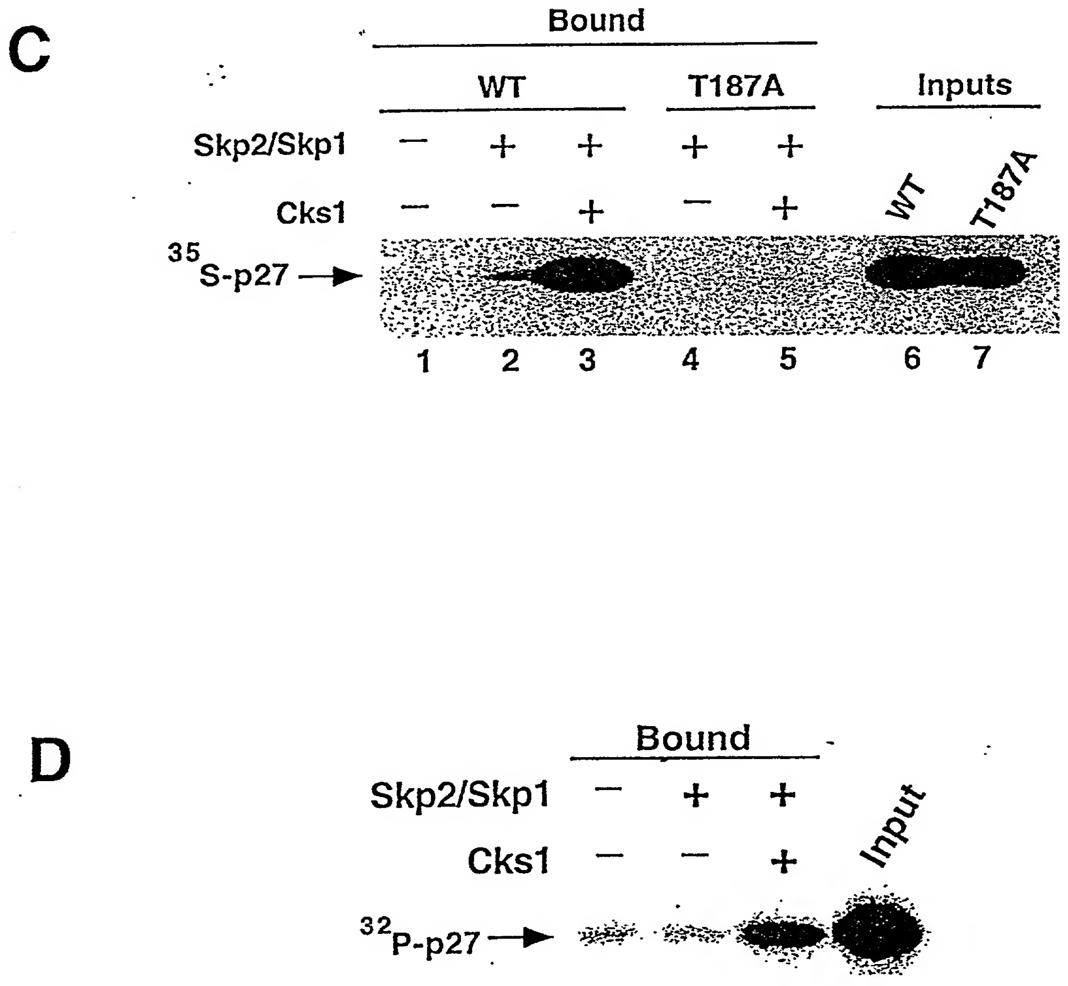
C
Bound
WT
T187A
Inputs
Skp2/Skp1
− + + + +
Cks1
− − + − +
WT
T187A
35S-p27
1 2 3 4 5 6 7
D
Bound
Skp2/Skp1
− + +
Cks1
− − +
Input
32P-p27

FIG. 49

5914-090

(SHEET 78 OF 80)

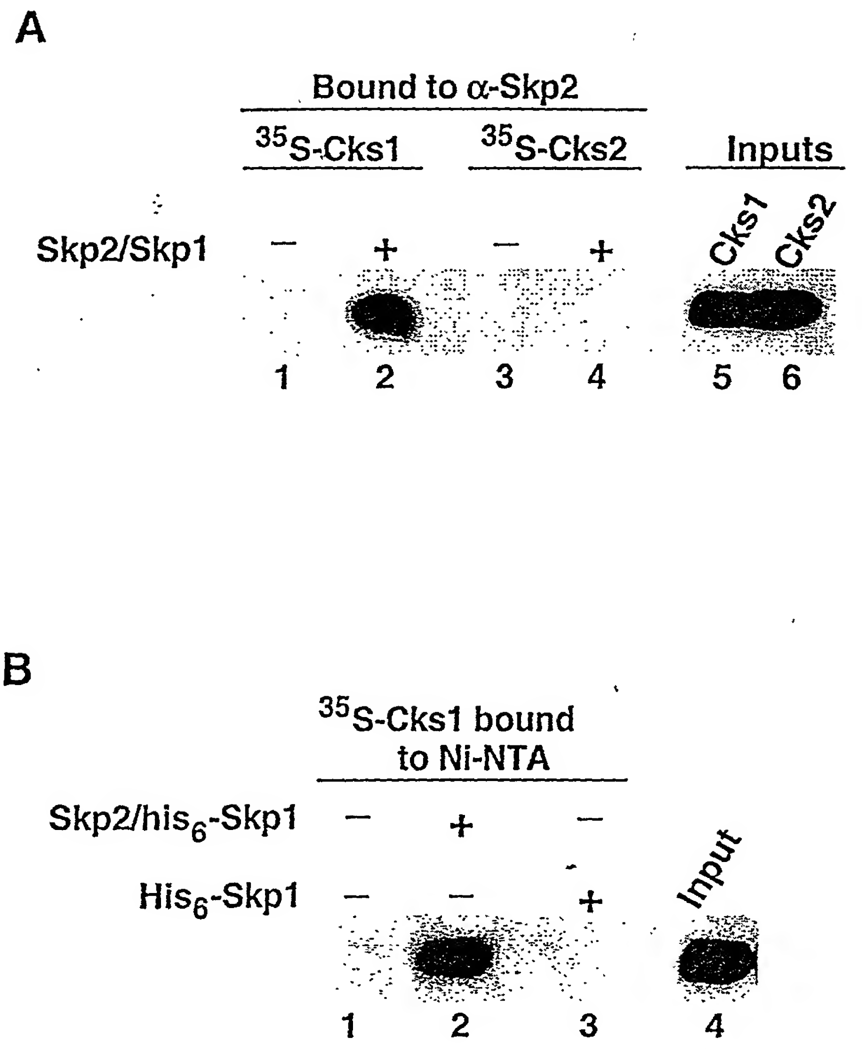

FIG. 5D

5914-090 (SHEET 79 OF 80)

FIG. 5D

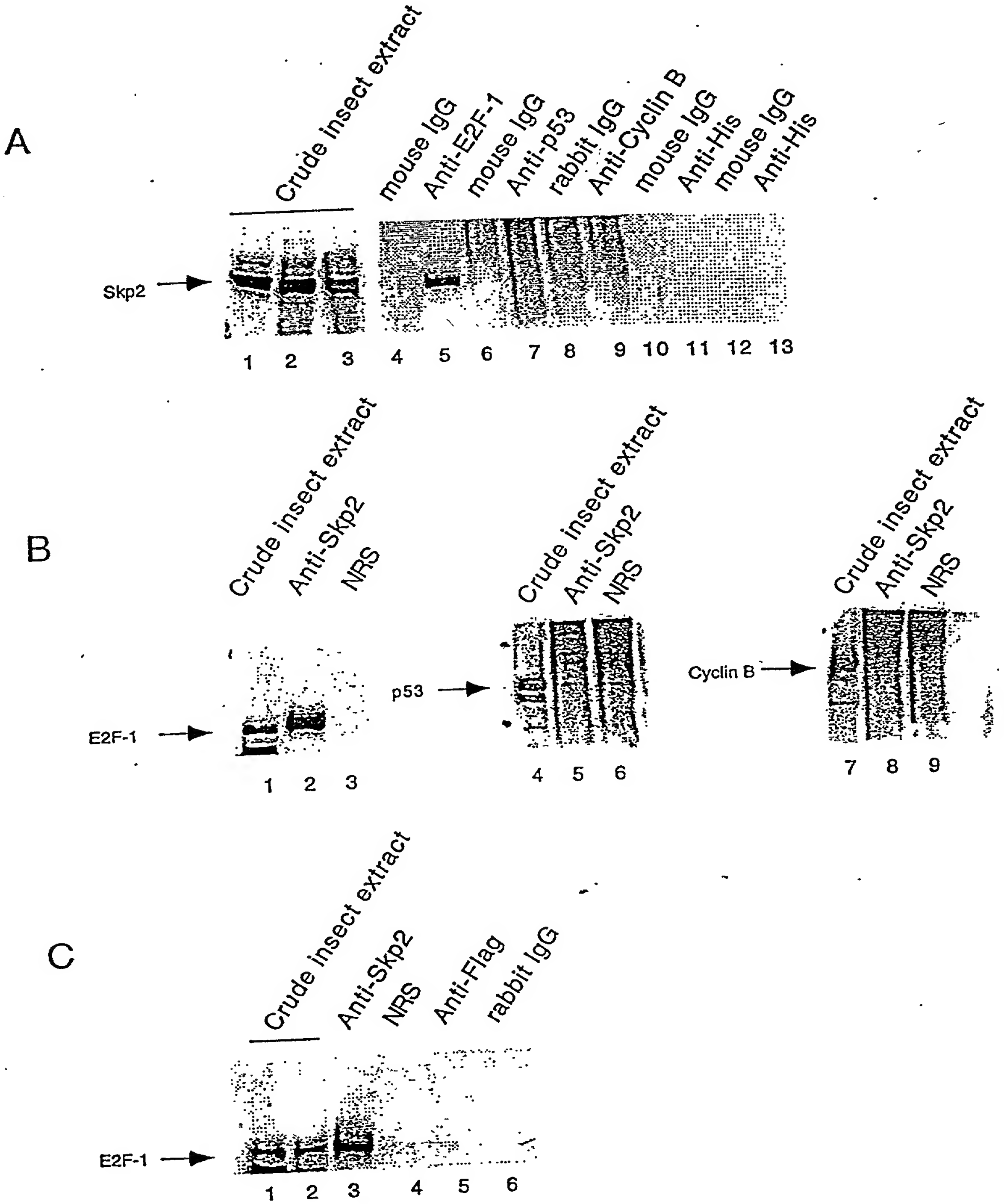
A
Crude insect extract
mouse IgG
Anti-E2F-1
mouse IgG
Anti-p53
rabbit IgG
Anti-Cyclin B
mouse IgG
Anti-His
mouse IgG
Anti-His
Skp2
1 2 3 4 5 6 7 8 9 10 11 12 13
B
Crude insect extract
Anti-Skp2
NRS
E2F-1
1 2 3
Crude insect extract
Anti-Skp2
NRS
p53
4 5 6
Crude insect extract
Anti-Skp2
NRS
Cyclin B
7 8 9
C
Crude insect extract
Anti-Skp2
NRS
Anti-Flag
rabbit IgG
E2F-1
1 2 3 4 5 6

FIG. 51 A-C